Stereoselective synthesis of oxazino[4,3-a]indoles employing oxa-Pictet-Spengler reaction of indoles bearing N-tethered vinylogous carbonate

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Experimental Procedures and Spectra

General Materials and Methods: Melting points are recorded using Tempo melting point apparatus in capillary tubes and are uncorrected. IR spectra were recorded on Nicolet 6700 spectrophotometers. ^{1}H (400 MHz) and ^{13}C (100 MHz) spectra were recorded on Bruker Avance 400 spectrometers. The chemical shifts (δ ppm) and coupling constants (Hz) are reported in the standard fashion with reference to internal tetramethylsilane, chloroform or benzene. In the ^{13}C NMR spectra, the nature of the carbons (C, CH, CH_2 or CH_3) was determined by recording the DEPT-135 experiment, and is given in parentheses. The NOESY (500 MHz) spectrums were recorded on Bruker Avance III 500 MHz (AV 500). High resolution mass measurements were carried out using Micromass Q-ToF GCMS instrument using direct inlet mode. Single crystal X-ray analysis was done on Bruker X8 Kappa APEX II. Analytical thin-layer chromatography (TLC) were performed on glass plates (7.5 x 2.5 and 7.5 x 5.0 cm) coated with Acme's silica gel G containing 13% calcium sulfate as binder or on pre-coated 0.2 mm thick Merck 60 F_{245} silica plates and various combinations of ethyl acetate and hexanes were used as eluent. Visualization of spots was accomplished by exposure to iodine vapor. All compounds were purified using silica gel [Acme's silica gel (100-200 mesh)] column chromatography and gave spectroscopic data consistent with being $\geq$ 95% the assigned structure. All small-scale dry reactions were carried out using standard syringe septum technique. Dry THF was obtained by distillation over sodium-benzophenone ketyl. Dry CH_2Cl_2 and dry DMF was prepared by distilling over calcium hydride. All the commercial reagents were used as such without further purification.

General Synthesis of Vinylogous carbonates 2:

Preparation of the alcohols 17 from the indoles 15:

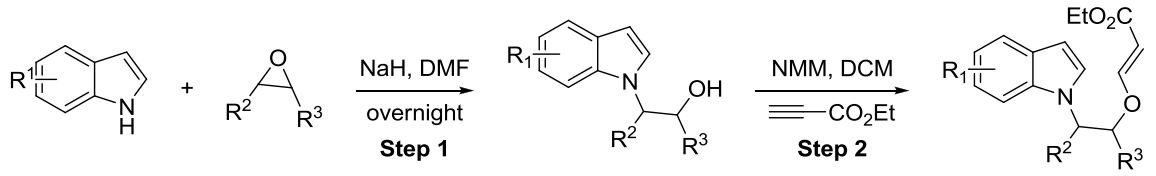
To a stirred solution of NaH (1 equiv) in dry DMF at 0 ^{o}C was added indole **15** (1 equiv) in dry DMF dropwise and stirred for about 20 min. The epoxide **16** (1 equiv) was added

at 0 ^{o}C and the reaction mixture was warmed to r.t. and stirred overnight. The reaction mixture was then quenched by adding water and extracted with ether. The combined organic extracts were washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexanes as the eluent furnished the corresponding alcohol **17**.

Preparation of the vinylogous carbonates 2 from the alcohols 17:

To a stirred solution of the alcohol **17** (1 equiv) in dry CH_2Cl_2, was added *N*-methylmorpholine (1 equiv) and ethylpropiolate (1.1 equiv) at r.t. and stirred until the completion of the reaction (*ca.* 4h, TLC control). The reaction mixture was then concentrated and purified by silica gel column chromatography using ethyl acetate-hexanes as the eluent to yield the requisite vinylogous carbonate **2**.

Table 1: Synthesis of vinylogous carbonates **2**



15 **16** **17** **2**

entry	R^1		R^2	R^3		product (Step 1)	yield (%)[a]	product (Step 2)	yield (%)[a]
1	H	**15a**	H	Me	**16a**	**17a**	85	**2a**	95
2	H	**15a**	H	Ph	**16b**	**17b**	91	**2b**	93
3	H	**15a**	H	CH_2OBn	**16c**	**17c**	74	**2c**	93
4	H	**15a**	$-(CH_2)_4-$		**16d**	**17d**	98[b]	**2d**	94
5	H	**15a**	$-(CH_2)_3-$		**16e**	**17e**	67[b]	**2e**	83
6	5-OMe	**15b**	H	Me	**16a**	**17f**	80	**2f**	78
7	5-OMe	**15b**	H	Ph	**16b**	**17g**	82	**2g**	85
8	5-Br	**15c**	H	Me	**16a**	**17h**	95[b]	**2h**	88
9	5-Br	**15c**	H	Ph	**16b**	**17i**	94	**2i**	78
10	3-Me	**15d**	H	Me	**16a**	**17j**	94	**2j**	82
11	3-Me	**15d**	H	Ph	**16b**	**17k**	78	**2k**	72
12	3-Ph	**15e**	H	Ph	**16b**	**17l**	77	**2l**	83
13	3-Ac	**15f**	H	Me	**16a**	**17m**	33	**2m**	83

[a] Yield corresponds to that of isolated, [b] Based on the recovered starting material

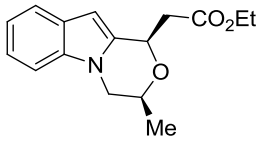
Preparation of oxazinoindoles 1a-l:

Ethyl [(1*R,3*S**)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1a):**

Using TMSOTf:

To a cold (0 ^{o}C), magnetically stirred solution of the vinylogous carbonate **2a** (24 mg, 0.087 mmol) in dry CH_2Cl_2 (4 mL) was added TMSOTf (25 μL, 0.1316 mmol). The reaction mixture was slowly allowed to warm up to r.t., stirred for 30 min. (TLC control) and quenched by adding saturated $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished a sticky solid, which was recrystallised from ethyl acetate-hexanes to furnish the oxazinoindole **1a** (22 mg, 92 %) as a white solid.

Physical appearance: white solid



R_f: 0.5 (1:9, EtOAc:Hexanes).

mp: 78 ^{o}C.

IR (neat): 2976, 2925, 1722, 1456, 1357, 1310, 1246, 1153, 1094, 1035, 953, 782, 740 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.56 (d, *J* = 7.8 Hz, 1H), 7.26 (d, *J* = 7.2 Hz, 1H), 7.18 (dt, *J* = 7.2, 0.9 Hz, 1H), 7.11 (dt, *J* = 7.2, 0.9 Hz, 1H), 6.20 (s, 1H), 5.35 (dd, *J* = 8.6, 4.2 Hz, 1H), 4.30-4.20 (m, 2H), 4.20-4.10 (m, 1H), 4.10 (ABX, *J* = 11.0, 3.2 Hz, 1H), 3.64 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.01 (ABX, *J* = 15.8, 4.2 Hz, 1H), 2.85 (ABX, *J* = 15.8, 8.6 Hz, 1H), 1.43 (d, *J* = 6.0 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.76 (C), 136.18 (C), 135.57 (C), 128.13 (C) 121.46 (CH), 120.62 (CH), 120.30 (CH), 108.84 (CH), 95.83 (CH), 71.37 (CH), 70.48 (CH), 60.95 (CH_2), 47.90 (CH_2), 40.53 (CH_2), 19.24 (CH_3), 14.37 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. for $C_{16}H_{20}NO_3$ 274.1443, found 274.1443.

Using $BF_3{\cdot}OEt_2$:

Reaction of the vinylogous carbonate **2a** (23 mg, 0.085 mmol) with $BF_3{\cdot}OEt_2$ (10 μL, 0.092 mmol) in dry CH_2Cl_2 (4 mL), as described for the synthesis of oxazinoindole **1a** using TMSOTf followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1a** (7 mg, 30 %) as a sticky solid.

Using $BiBr_3$:

Reaction of the vinylogous carbonate **2a** (11 mg, 0.040 mmol) with $BiBr_3$ (20 mg, 0.044 mmol) in dry CH_2Cl_2 (4 mL), as described for the synthesis of oxazinoindole **1a** using TMSOTf followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1a** (6 mg, 54 %) as a sticky solid.

Using $TiCl_4$:

Reaction of the vinylogous carbonate **2a** (51 mg, 0.187 mmol) with $TiCl_4$ (25 μL, 0.205 mmol) in dry CH_2Cl_2 (4 mL), as described for the synthesis of oxazinoindole **1a** using TMSOTf followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1a** (21 mg, 42 %) as a sticky solid.

Using $SnCl_4$:

Reaction of the vinylogous carbonate **2a** (44 mg, 0.160 mmol) with $SnCl_4$ (20 μL, 0.177 mmol) in dry CH_2Cl_2 (4 mL), as described for the synthesis of oxazinoindole **1a** using TMSOTf followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1a** (24 mg, 56 %) as a sticky solid.

Using $FeCl_3$:

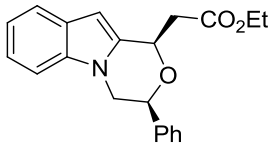
Reaction of the vinylogous carbonate **2a** (51 mg, 0.186 mmol) with $FeCl_3$ (50 mg, 0.300 mmol) in dry CH_2Cl_2 (4 mL), as described for the synthesis of oxazinoindole **1a** using TMSOTf followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1a** (27 mg, 53 %) as a sticky solid.

Using CF_3CO_2H:

Reaction of the vinylogous carbonate **2a** (53 mg, 0.194 mmol) with CF_3CO_2H (30 μL, 0.388 mmol) in dry CH_2Cl_2 (4 mL), as described for the synthesis of oxazinoindole **1a** using TMSOTf followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1a** (21 mg, 42 %) as a sticky solid.

Ethyl [(1*R,3*S**)-3-phenyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1b):**

Reaction of the vinylogous carbonate **2b** (110 mg, 0.328 mmol) with TMSOTf (65 μL, 0.360 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1b** (67 mg, 61 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 2980, 2928, 1733, 1608, 1459, 1366, 1324, 1168, 1103, 1059, 1038, 932, 780, 746 cm^{-1}.

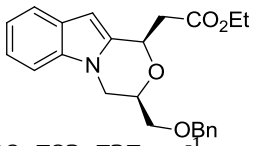
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (d, *J* = 7.8 Hz, 1H), 7.55-7.45 (m, 2H), 7.45-7.30 (m, 3H), 7.27 (d, *J* = 7.3 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.14 (t, *J* = 7.2 Hz, 1H), 6.28 (s, 1H), 5.57 (dd, *J* = 8.2, 4.5 Hz, 1H), 5.08 (dd, *J* = 11.5, 3.5 Hz, 1H), 4.36 (ABX, *J* = 11.5, 3.5 Hz, 1H), 4.24 (q, *J* = 7.1 Hz, 2H), 3.92 (ABX, *J* = 11.5, 11.5 Hz, 1H), 3.11 (ABX, *J* = 15.8, 4.5 Hz, 1H), 2.99 (ABX, *J* = 15.8, 8.2 Hz, 1H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.60 (C), 138.87 (C), 136.28 (C), 135.35 (C), 128.76 (CH, 2C), 128.52 (CH), 128.20 (C), 126.15 (CH, 2C), 121.62 (CH), 120.70 (CH), 120.44 (CH), 108.88 (CH), 96.21 (CH), 76.12 (CH), 71.94 (CH), 60.96 (CH_2), 48.07 (CH_2), 40.70 (CH_2), 14.36 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. For $C_{21}H_{22}NO_3$ 336.1600, found 336.1604.

Ethyl [(1*R,3*R**)-3-(benzyloxymethyl)-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1c):**

Reaction of the vinylogous carbonate **2c** (63 mg, 0.166 mmol) with TMSOTf (35 μL, 0.182 mmol) in dry CH_2Cl_2 (5 mL) for 1.5 h, as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1c** (38 mg, 60 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 2922, 2860, 1731, 1617, 1457, 1367, 1313, 1283, 1172, 1095, 1029, 783, 737 cm^{-1}.

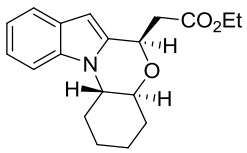
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (d, *J* = 7.9 Hz, 1H), 7.35-7.15 (m, 6H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.13 (s, 1H), 5.31 (dd, *J* = 8.4, 4.3 Hz, 1H), 4.57 (s, 2H), 4.25-4.10 (m, 4H), 3.80-3.70 (m, 2H), 3.63 (ABX, *J* = 10.3, 5.4 Hz, 1H), 2.96 (ABX, *J* = 15.9, 4.3 Hz, 1H), 2.80 (ABX, *J* = 15.9, 8.4 Hz, 1H), 1.22 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.61 (C), 137.94 (C), 136.36 (C), 135.42 (C), 128.62 (CH, 2C), 128.00 (CH), 127.94 (CH), 127.90 (CH, 2C), 121.54 (CH), 120.62 (CH), 120.34 (CH), 108.94 (CH), 95.96 (CH), 73.81 (CH_2), 73.58 (CH), 71.54 (CH), 70.80 (CH_2), 60.98 (CH_2), 44.05 (CH_2), 40.42 (CH_2), 14.36 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{23}H_{26}NO_4$ 380.1862, found 380.1865.

Ethyl [4a*S,12a*S**]-1,2,3,4,4a,12a,-hexahydro-6*H*,indolo[2,1-*c*][1,4]benzoxazin-6-yl-acetate (1d):**

Reaction of the vinylogous carbonate **2d** (50 mg, 0.159 mmol) with TMSOTf (30 μL, 0.176 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1d** (28 mg, 56 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R$_f$: 0.6 (1:9, EtOAc:Hexanes).

IR (neat): 2934, 2864, 1734, 1455, 1327, 1240, 1171, 1109, 1036, 784, 744 cm^{-1}.

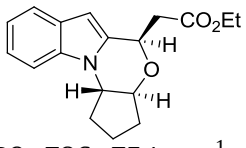
^{1}H NMR (400MHz, CDCl$_3$): δ 7.48 (d, *J* = 7.2 Hz, 1H), 7.43 (d, *J* = 8.4 Hz, 1H), 7.10-7.05 (m, 2H), 6.20 (s, 1H), 5.39 (dd, *J* = 8.5, 4.2 Hz, 1H), 4.30-4.20 (m, 2H), 3.93 (dt, *J* = 10.5, 3.5 Hz, 1H), 3.64 (dt, *J* = 10.5, 3.5 Hz, 1H), 3.25-3.05 (m, 1H), 3.00 (ABX, *J* = 15.8, 4.2 Hz, 1H), 2.82 (ABX, *J* = 15.8, 8.5 Hz, 1H), 2.20-2.10 (m, 1H), 2.00-1.80 (m, 2H), 1.70-1.44 (m, 4H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100MHz, CDCl$_3$, DEPT): δ 170.77 (C), 137.48 (C), 136.53 (C), 128.79 (C), 121.28 (CH), 120.70 (CH), 119.88 (CH), 111.81 (CH), 96.76 (CH), 80.49 (CH), 72.33 (CH), 60.94 (CH_2), 59.78 (CH), 40.75 (CH_2), 31.29 (CH_2), 30.16 (CH_2), 24.70 (CH_2), 24.55 (CH_2), 14.36 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{19}H_{24}NO_3$ 314.1756, found 314.1752.

Ethyl [3*aS,5*R**,11*aS**]-2,3,3*a*,11*a*-tetrahydro-1*H*,5*H*-cyclopenta[5,6][1,4]oxazino[4,3-*a*]indol-5yl-acetate (1e):**

Reaction of the vinylogous carbonate **2e** (130 mg, 0.434 mmol) with TMSOTf (120 μL, 0.651 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1e** (41 mg, 32 %) as a syrupy liquid.



Physical appearance: yellow oil

R$_f$: 0.6 (1:9, EtOAc:Hexanes).

IR (neat): 2968, 1732, 1618, 1461, 1368, 1330, 1288, 1166, 1124, 1029, 786, 754 cm^{-1}.

^{1}H NMR (400MHz, CDCl$_3$): δ 7.56 (d, *J* = 7.7 Hz, 1H), 7.38 (d, *J* = 8.0 Hz, 1H), 7.16 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.10 (dt, *J* = 8.0, 1.0 Hz, 1H), 6.25 (s, 1H), 5.50 (dd, *J* = 8.1, 4.2

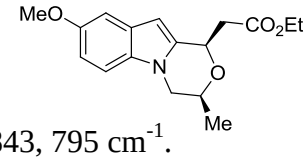
Hz, 1H), 4.30-4.15 (m, 2H), 3.95-3.85 (m, 1H), 3.85-3.75 (m, 1H), 3.05 (ABX, *J* = 15.9, 4.2 Hz, 1H), 2.91 (ABX, *J* = 15.9, 8.1 Hz, 1H), 2.80-2.65 (m, 1H), 2.15-1.90 (m, 4H), 1.80-1.65 (m, 1H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 170.67 (C), 137.07 (C), 136.72 (C), 128.19 (C), 121.73 (CH), 120.69 (CH), 120.10 (CH), 110.77 (CH), 97.82 (CH), 82.15 (CH), 72.73 (CH), 60.96 (CH_2), 59.04 (CH), 40.85 (CH_2), 25.67 (CH_2), 25.18 (CH_2), 18.33 (CH_2), 14.34 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{18}H_{22}NO_3$ 300.1600, found 300.1594.

Ethyl [(1*R,3*S**)-8-methoxy-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1f):**

Reaction of the vinylogous carbonate **2f** (210 mg, 0.692 mmol) with TMSOTf (140 μL, 0.761 mmol) in dry CH_2Cl_2 (8 mL) for 1.5 h, as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1f** (194 mg, 92 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 2980, 1733, 1620, 1477, 1361, 1288, 1168, 1096, 1034, 950, 843, 795 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, *J* = 8.8 Hz, 1H), 7.04 (d, *J* = 2.4 Hz, 1H), 6.85 (dd, *J* = 8.8, 2.4 Hz, 1H), 6.13 (s, 1H), 5.33 (dd, *J* = 8.6, 4.2 Hz, 1H), 4.25 (q, *J* = 7.1 Hz, 2H), 4.15-4.05 (m, 1H), 4.04 (ABX, *J* = 11.0, 3.3 Hz, 1H), 3.84 (s, 3H), 3.61 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.00 (ABX, *J* = 15.8, 4.2 Hz, 1H), 2.84 (ABX, *J* = 15.8, 8.6 Hz, 1H), 1.42 (d, *J* = 6.2 Hz, 3H), 1.31 (t, *J* = 7.1 Hz, 3H).

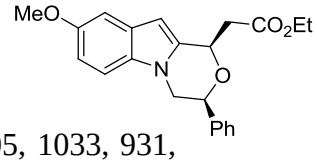
^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.77 (C), 154.65 (C), 136.09 (C), 131.46 (C), 128.4 (C), 111.52 (CH), 109.48 (CH), 102.55 (CH), 95.48 (CH), 71.27 (CH), 70.41 (CH), 60.94 (CH_2), 56.02 (CH_3), 47.87 (CH_2), 40.43 (CH_2), 19.19 (CH_3), 14.35 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{17}H_{22}NO_4$ 304.1549, found 304.1553.

Ethyl [(1*R,3*S**)-8-methoxy-3-phenyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1g):**

Reaction of the vinylogous carbonate **2g** (60 mg, 0.164 mmol) with TMSOTf (40 μL, 0.246 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1a**

followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1g** (43 mg, 72 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 2938, 1732, 1619, 1578, 1478, 1443, 1287, 1167, 1105, 1033, 931, 843, 794, 761 cm^{-1}.

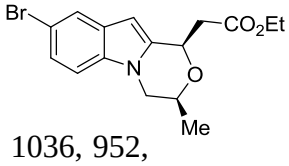
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50-7.35 (m, 5H), 7.15 (d, *J* = 8.8 Hz, 1H), 7.08 (d, *J* = 2.3 Hz, 1H), 6.87 (dd, *J* = 8.8, 2.3 Hz, 1H), 6.21 (s, 1H), 5.54 (dd, *J* = 8.1, 4.5 Hz, 1H), 5.05 (dd, *J* = 11.0, 3.4 Hz, 1H), 4.30 (ABX, *J* = 11.0, 3.4 Hz, 1H), 4.27 (q, J = 7.2 Hz, 2H), 3.88 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.86 (s, 3H), 3.10 (ABX, *J* = 15.7, 4.5 Hz, 1H), 2.98 (ABX, *J* = 15.7, 8.1 Hz, 1H), 1.30 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.57 (C), 154.81 (C), 138.87 (C), 135.94 (C), 131.61 (C), 128.74 (CH, 2C), 128.59 (CH), 128.50 (CH), 126.13 (CH, 2C), 111.70 (CH), 109.51 (CH), 102.76 (CH), 95.90 (CH), 76.08 (CH), 71.88 (CH), 60.93 (CH_2), 56.04 (CH_3), 48.09 (CH_2), 40.66 (CH_2), 14.36 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. For $C_{22}H_{24}NO_4$ 366.1705, found 366.1707.

Ethyl [(1*R,3*S**)-8-bromo-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1h):**

Reaction of the vinylogous carbonate **2h** (120 mg, 0.341 mmol) with TMSOTf (100 μL, 0.511 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1h** (65 mg, 54 %) as a syrupy liquid.



Physical appearance: brown syrupy liquid

R_f: 0.6 (1:9, EtOAc:Hexanes).

IR (neat): 2972, 2927, 1722, 1454, 1363, 1312, 1243, 1153, 1095, 1036, 952, 893, 852, 792, 730 cm^{-1}.

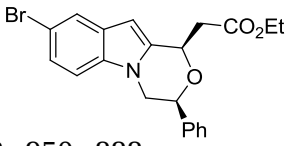
^{1}H NMR (400 MHz, $CDCl_3$): δ 7.68 (d, *J* = 1.8 Hz, 1H), 7.26 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.12 (d, *J* = 8.6 Hz, 1H), 6.14 (s, 1H), 5.33 (dd, *J* = 8.4, 4.2 Hz, 1H), 4.30-4.20 (m, 2H), 4.20-4.10 (m, 1H), 4.06 (ABX, *J* = 11.1, 3.3 Hz, 1H), 3.63 (ABX, *J* = 11.1, 11.1 Hz, 1H), 2.99 (ABX, *J* = 15.9, 4.2 Hz, 1H), 2.85 (ABX, *J* = 15.9, 8.4 Hz, 1H), 1.43 (d, *J* = 6.2 Hz, 3H), 1.30 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100 MHz, $CDCl_3$, DEPT): δ 170.55 (C), 136.73 (C), 134.79, (C), 129.71 (C), 124.22 (CH), 123.06 (CH), 113.40 (C), 110.21 (CH), 95.44 (CH), 71.15 (CH), 70.35 (CH), 60.99 (CH_2), 47.80 (CH_2), 40.36 (CH_2), 19.16 (CH_3), 14.34 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{16}H_{19}NO_3Br$ 352.0548, found 352.0548.

Ethyl [(1*R,3*S**)-8-bromo-3-phenyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1i):**

Reaction of the vinylogous carbonate **2i** (190 mg, 0.459 mmol) with TMSOTf (130 μL, 0.688 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1i** (121 mg, 64 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 2929, 1731, 1455, 1364, 1318, 1266, 1171, 1102, 1038, 950, 888, 788, 734, 695 cm^{-1}.

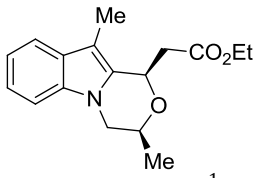
^{1}H NMR (400MHz, $CDCl_3$): δ 7.63 (d, *J* = 1.3 Hz, 1H), 7.45-7.15 (m, 6H), 7.04 (d, *J* = 8.6 Hz, 1H), 6.13 (s, 1H), 5.46 (dd, *J* = 8.0, 4.6 Hz, 1H), 4.98 (dd, *J* = 11.3, 3.5 Hz, 1H), 4.23 (ABX, *J* = 11.3, 3.5 Hz, 1H), 4.15 (q, *J* = 7.1 Hz, 2H), 3.82 (ABX, *J* = 11.3, 11.3 Hz, 1H), 3.00 (ABX, *J* = 15.9, 4.6 Hz, 1H), 2.90 (ABX, *J* = 15.9, 8.0 Hz, 1H), 1.21 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 170.42 (C), 138.54 (C), 136.53 (C), 134.90 (C), 129.80 (C), 128.81 (CH, 2C), 128.65 (CH), 126.11 (CH, 2C), 124.44 (CH), 123.18 (CH), 113.58 (C), 110.25 (CH), 95.82 (CH), 76.01 (CH), 71.76 (CH), 61.04 (CH_2), 48.04 (CH_2), 40.55 (CH_2), 14.35 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{21}H_{21}BrNO_3$ 414.0705, found 414.0705.

Ethyl [(1*R,3*S**)-3,10-dimethyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1j):**

Reaction of the vinylogous carbonate **2j** (62 mg, 0.216 mmol) with TMSOTf (45 μL, 0.237 mmol) in dry CH_2Cl_2 (6 mL) for 40 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1j** (53 mg, 85 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 2979, 2930, 1729, 1614, 1460, 1366, 1241, 1158, 1095, 1036, 849, 746, 605 cm^{-1}.

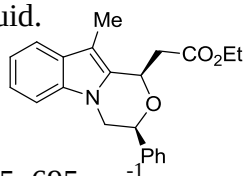
^{1}H NMR (400MHz, $CDCl_3$): δ 7.44 (d, *J* = 7.9 Hz, 1H), 7.20-7.00 (m, 3H), 5.38 (dd, *J* = 9.5, 2.5 Hz, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 3.95 (ABX, *J* = 11.0, 3.0 Hz, 1H), 3.95-3.80 (m, 1H), 3.60 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.12 (ABX, *J* = 15.6, 2.5 Hz, 1H), 2.70 (ABX, *J* = 15.6, 9.5 Hz, 1H), 2.19 (s, 3H), 1.31 (d, *J* = 6.2 Hz, 3H), 1.20 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 170.83 (C), 135.30 (C), 129.94 (C), 128.81 (C), 121.33 (CH), 119.46 (CH), 118.40 (CH), 108.44 (CH), 103.86 (CH), 71.27 (CH), 70.06 (CH), 60.77 (CH_2), 47.97 (CH_2), 40.65 (CH_2), 19.02 (CH_3), 14.33 (CH_3), 9.38 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. For $C_{17}H_{22}NO_3$ 288.1600, found 288.1606.

Ethyl [(1*R,3*S**)-10-methyl-3-phenyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1k):**

Reaction of the vinylogous carbonate **2k** (60 mg, 0.172 mmol) with TMSOTf (35 μL, 0.189 mmol) in dry CH_2Cl_2 (6 mL) for 1 h, as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:24) as eluent furnished the oxazinoindole **1k** (67 mg, 61 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.6 (1:9, EtOAc:Hexanes).

IR (neat): 2926, 1729, 1615, 1459, 1367, 1240, 1162, 1098, 1031, 735, 695 cm^{-1}.

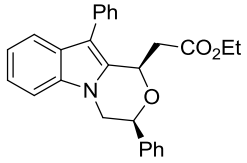
^{1}H NMR (400MHz, $CDCl_3$): δ 7.85 (d, *J* = 7.6 Hz, 1H), 7.80-7.75 (m, 2H), 7.75-7.60 (m, 3H), 7.55-7.40 (m, 3H), 5.96 (dd, *J* = 9.1, 3.0 Hz, 1H), 5.20 (dd, *J* = 11.0, 3.0 Hz, 1H), 4.60 (ABX, *J* = 11.0, 3.0 Hz, 1H), 4.55-4.40 (m, 2H), 4.24 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.56 (ABX, *J* = 15.4, 3.0 Hz, 1H), 3.22 (ABX, *J* = 15.4, 9.1 Hz, 1H), 2.62 (s, 3H), 1.55 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 170.68 (C), 138.82 (C), 135.35 (C), 129.66 (C), 128.82 (C), 128.67 (CH, 2C), 128.40 (CH), 126.09 (CH, 2C), 121.51 (CH), 119.61 (CH), 118.52 (CH), 108.49 (CH), 104.28 (CH), 75.63 (CH), 71.73 (CH), 60.85 (CH_2), 48.33 (CH_2), 40.90 (CH_2), 14.35 (CH_3), 9.38 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. for $C_{22}H_{24}NO_3$ 350.1756, found 350.1759.

Ethyl [(1*R,3*S**)-3,10-diphenyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1l):**

Reaction of the vinylogous carbonate **2l** (55 mg, 0.134 mmol) with TMSOTf (25 μL, 0.142 mmol) in dry CH_2Cl_2 (6 mL) for 35 min., as described for the oxazinoindole **1a** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1l** (40 mg, 74 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:9, EtOAc:Hexanes).

IR (neat): 3051, 2930, 1733, 1605, 1458, 1370, 1281, 1245, 1170, 1104, 1026, 965, 928, 749, 695 cm^{-1}.

^{1}H NMR (400MHz, $CDCl_3$): δ 7.65 (d, *J* = 7.8 Hz, 2H), 7.55-7.30 (m, 11H), 7.20-7.10 (m, 1H), 5.97 (dd, *J* = 9.2, 2.4 Hz, 1H), 5.10 (dd, *J* = 11.0, 3.0 Hz, 1H), 4.43 (ABX, *J* = 11.0, 3.0 Hz, 1H), 4.15-4.00 (m, 3H), 2.88 (ABX, *J* = 15.9, 2.4 Hz, 1H), 2.57 (ABX, *J* = 15.9, 9.2 Hz, 1H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 170.79 (C), 138.73 (C), 135.37 (C), 135.01 (C), 130.36 (C), 129.84 (CH, 2C), 128.89 (CH, 2C), 128.75 (CH, 2C), 128.51 (CH), 127.61 (C), 126.68 (CH), 126.09 (CH, 2C), 122.08 (CH), 120.71 (CH), 119.42 (CH), 111.97 (C), 108.73 (CH), 75.45 (CH), 72.17 (CH), 60.66 (CH_2), 48.25 (CH_2), 39.63 (CH_2), 14.28 (CH_3).

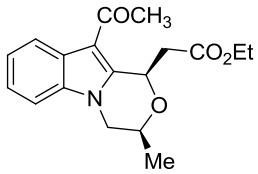
HRMS (ESI, M+H^+): m/z calcd. for $C_{27}H_{26}NO_3$ 412.1913, found 412.1914.

Procedure for the preparation of oxazinoindoles 1m-u:

Ethyl [(1*R,3*S**)-10-acetyl-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1m):**

To a cold (0 ^oC), magnetically stirred solution of the vinylogous carbonate **2a** (51 mg, 0.187 mmol) in dry CH_2Cl_2 (6 mL) was added TMSOTf (40 μL, 0.224 mmol). The reaction mixture was slowly allowed to warm up to r.t. and stirred for 30 min. After the vinylogous carbonate was completely consumed (TLC control), Ac_2O (35 μL, 0.373 mmol) was added at r.t. and stirred for 3 h. After completion of the reaction, quenched by adding saturated $NaHCO_3$. The reaction mixture was extracted with CH_2Cl_2 (3 x 10 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent and purification

of the residue on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1m** (44 mg, 75 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.3 (1:3, EtOAc:Hexanes).

IR (neat): 2979, 2928, 1732, 1634, 1493, 1460, 1427, 1373, 1290, 1160, 1093, 1025, 966, 739 cm^{-1}.

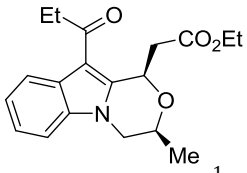
^{1}H NMR (400MHz, $CDCl_3$): δ 7.84 (dd, *J* = 7.0, 1.5 Hz, 1H), 7.30-7.10 (m, 3H), 5.71 (dd, *J* = 6.3, 3.4 Hz, 1H), 4.10-3.90 (m, 3H), 3.90-3.80 (m, 1H), 3.75 (ABX, *J* = 10.5, 10.5 Hz, 1H), 3.22 (ABX, *J* = 16.3, 3.4 Hz, 1H), 2.97 (ABX, *J* = 16.3, 6.3 Hz, 1H), 2.62 (s, 3H), 1.34 (d, *J* = 6.1 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 193.65 (C), 170.92 (C), 144.16 (C), 136.09 (C), 126.21 (C), 122.79 (CH), 122.35 (CH), 120.68 (CH), 112.38 (C), 109.69 (CH), 72.07 (CH), 68.99 (CH), 60.42 (CH_2), 48.26 (CH_2), 39.53 (CH_2), 31.44 (CH_3), 18.80 (CH_3), 14.27 (CH_3).

HRMS (ESI, $M+H^+$): m/z calcd. for $C_{18}H_{22}NO_4$ 316.1549, found 316.1545.

Ethyl [(1*R,3*S**)-3-methyl-10-propionyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1n):**

Reaction of the vinylogous carbonate **2a** (42 mg, 0.154 mmol) with TMSOTf (40 μL, 0.230 mmol) and propionic anhydride (40 μL, 0.307 mmol) in dry CH_2Cl_2 (6 mL) for 6 h, as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1n** (38 mg, 77 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.3 (1:4, EtOAc:Hexanes).

IR (neat): 2976, 2935, 1734, 1639, 1492, 1459, 1373, 1268, 1166, 1098, 1042, 960, 752 cm^{-1}.

^{1}H NMR (400MHz, $CDCl_3$): δ 7.91 (br d, *J* = 8.4 Hz, 1H), 7.40-7.25 (m, 3H), 5.80 (dd, *J* = 6.2, 3.4 Hz, 1H), 4.15-4.00 (m, 3H), 4.00-3.90 (m, 1H), 3.82 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.30 (ABX, *J* = 16.2, 3.4 Hz, 1H), 3.15-3.00 (m, 3H), 1.41 (d, *J* = 6.0 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.18 (t, *J* = 7.2 Hz, 3H).

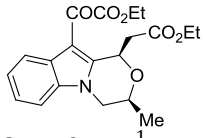
^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 196.85 (C), 170.96 (C), 144.08 (C), 136.09 (C), 125.76 (C), 122.70 (CH), 122.26 (CH), 120.98 (CH), 112.01 (C), 109.66 (CH), 72.13

(CH), 68.96 (CH), 60.41 (CH_2), 48.27 (CH_2), 39.52 (CH_2), 36.22 (CH_2), 18.80 (CH_3), 14.26 (CH_3), 8.28 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{19}H_{24}NO_4$ 330.1705, found 330.1710.

Ethyl [(1*R,3*S**)-1-(2-ethoxy-2-oxoethyl)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-10-yl)-2-oxoacetate (1o):**

Reaction of the vinylogous carbonate **2a** (98 mg, 0.358 mmol) with TMSOTf (100 μL, 0.538 mmol) and ethylchlorooxoacetate (100 μL, 0.732 mmol) in dry CH_2Cl_2 (8 mL) for 6 h, as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1a** (42 mg, 43 %) and **1o** (59 mg, 36 %, 77% based on recovered **1a**) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.3 (1:4, EtOAc:Hexanes).

IR (neat): 2925, 1731, 1623, 1458, 1373, 1262, 1184, 1092, 1018, 964, 858, 750 cm^{-1}.

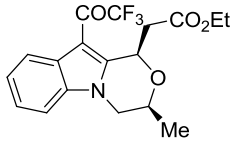
^{1}H NMR (400MHz, $CDCl_3$): δ 7.60-7.55 (m, 1H), 7.30-7.15 (m, 3H), 5.66 (dd, *J* = 6.0, 3.4 Hz, 1H), 4.41 (q, *J* = 7.1 Hz, 2H), 4.10-3.95 (m, 3H), 3.95-3.80 (m, 1H), 3.85-3.70 (m, 1H), 3.21 (ABX, *J* = 16.6, 3.4 Hz, 1H), 3.05 (ABX, *J* = 16.6, 6.2 Hz, 1H), 1.40-1.30 (m, 6H), 1.11 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 180.53 (C), 170.45 (C), 166.22 (C), 147.37 (C), 136.20 (C), 125.72 (C), 123.72 (CH), 123.32 (CH), 119.79 (CH), 109.81 (CH), 107.24 (C), 71.65 (CH), 69.06 (CH), 62.23 (CH_2), 60.60 (CH_2), 48.22 (CH_2), 39.27 (CH_2), 18.70 (CH_3), 14.22 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{20}H_{24}NO_6$ 374.1604, found 374.1606.

Ethyl [(1*R,3*S**)-3-methyl-10-(2,2,2-trifluoroacetyl)-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1p):**

Reaction of the vinylogous carbonate **2a** (21 mg, 0.077 mmol) with TMSOTf (20 μL, 0.115 mmol) and TFAA (40 μL, 0.230 mmol) in dry CH_2Cl_2 (4 mL) for 4 h, as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1a** (11 mg, 52 %) and **1p** (9 mg, 32 %, 69% based on recovered **1a**) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:4, EtOAc:Hexanes).

IR (neat): 2935, 2253, 1735, 1652, 1476, 1381, 1273, 1192, 1147, 1094, 913, 741 cm^{-1}.

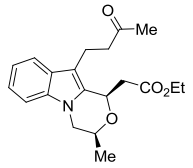
^{1}H NMR (400MHz, $CDCl_3$): δ 7.99 (d, *J* = 7.2 Hz, 1H), 7.40-7.30 (m, 3H), 5.76 (dd, *J* = 4.8, 4.3 Hz, 1H), 4.20-4.00 (m, 3H), 4.00-3.90 (m, 1H), 3.87 (ABX, *J* = 11.5, 10.4 Hz, 1H), 3.18 (ABX, *J* = 16.6, 3.6 Hz, 1H), 3.07 (ABX, *J* = 16.6, 5.6 Hz, 1H), 1.44 (d, *J* = 6.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 174.17 (q, *J* = 36.4 Hz, CO), 170.41 (C), 150.41 (C), 136.42 (C), 124.31 (C), 124.10 (CH), 123.61 (CH), 121.19 (CH), 121.14 (CH), 117.40 (q, *J* = 287.4 Hz, CF_3), 109.82 (CH), 106.11 (C), 71.90 (CH), 68.93 (CH), 60.63 (CH_2), 48.33 (CH_2), 38.67 (CH_2), 18.61 (CH_3), 14.16 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. for $C_{18}H_{19}NO_4F_3$ 370.1266, found 370.1261.

Ethyl [(1*R,3*S**)-3-methyl-10-(3-oxobutyl)-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1q):**

To a cold (0 ^oC), magnetically stirred solution of the vinylogous carbonate **2a** (13 mg, 0.048 mmol) and methyl vinyl ketone (10 μL, 0.110 mmol) in dry CH_2Cl_2 (6 mL) was added TMSOTf (15 μL, 0.071 mmol) in two portions over a period of 30 min. The reaction mixture was quenched by adding saturated $NaHCO_3$, extracted with CH_2Cl_2 (3 x 5 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1q** (11 mg, 69 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:3, EtOAc:Hexanes).

IR (neat): 2926, 2857, 1722, 1613, 1461, 1366, 1268, 1158, 1029, 973, 902, 855, 743 cm^{-1}.

^{1}H NMR (400MHz, $CDCl_3$): δ 7.41 (d, *J* = 8.0 Hz, 1H), 7.14 (d, *J* = 8.0 Hz, 1H), 7.09 (td, *J* = 8.1, 1.0 Hz, 1H), 7.02 (td, *J* = 8.0, 1.0 Hz, 1H), 5.21 (dd, *J* = 9.0, 3.1 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.95 (ABX, *J* = 11.0, 2.9 Hz, 1H), 3.95-3.80 (m, 1H), 3.60 (t, *J* = 11.0 Hz, 1H), 3.08 (ABX, *J* = 15.5, 3.1 Hz, 1H), 2.95-2.80 (m, 2H), 2.80-2.65 (m, 2H), 2.65-2.50 (m, 1H), 2.03 (s, 3H), 1.30 (d, *J* = 6.2 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H).

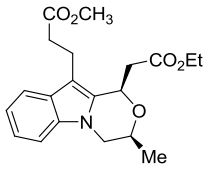
^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 208.36 (C), 170.62 (C), 135.50 (C), 130.24 (C), 127.75 (C), 121.52 (CH), 119.69 (CH), 118.42 (CH), 108.71 (CH), 107.67 (C), 71.14

(CH), 69.96 (CH), 60.85 (CH_2), 47.99 (CH_2), 44.43 (CH_2), 40.91 (CH_2), 30.22 (CH_3), 19.02 (CH_2), 18.68 (CH_3), 14.34 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{20}H_{26}NO_4$ 344.1862, found 344.1861.

Methyl [(1*R,3*S**)-1-(2-ethoxy-2-oxoethyl)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-10-yl]propanoate (1r):**

Reaction of the vinylogous carbonate **2a** (80 mg, 0.293 mmol) with TMSOTf (100 μL, 0.585 mmol) and methylacrylate (100 μL, 1.097 mmol) in dry CH_2Cl_2 (6 mL) for 19 h, as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1r** (72 mg, 69 %) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (1:4, EtOAc:Hexanes).

IR (neat): 2937, 1733, 1613, 1459, 1363, 1253, 1166, 1097, 1033, 746 cm^{-1}.

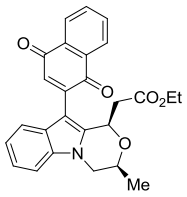
^{1}H NMR (400MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.8 Hz, 1H), 7.25-7.15 (m, 2H), 7.12 (dt, *J* = 8.0, 1.0 Hz, 1H), 5.48 (dd, *J* = 9.2, 3.0 Hz, 1H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.06 (ABX, *J* = 11.3, 2.9 Hz, 1H), 4.00-3.95 (m, 1H), 3.70 (ABX, *J* = 10.9, 10.9 Hz, 1H), 3.68 (s, 3H), 3.18 (ABX, *J* = 15.4, 3.0 Hz, 1H), 3.10-2.95 (m, 2H), 2.81 (ABX, *J* = 15.4, 9.2 Hz, 1H), 2.75-2.60 (m, 1H), 2.60-2.50 (m, 1H), 1.44 (d, *J* = 6.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 173.56 (C), 170.60 (C), 135.47 (C), 130.34 (C), 127.72 (C), 121.56 (CH), 119.77 (CH), 118.47 (CH), 108.71 (CH), 107.31 (C), 71.12 (CH), 69.97 (CH), 60.87 (CH_2), 51.82 (CH_3), 47.97 (CH_2), 40.87 (CH_2), 35.14 (CH_2), 20.28 (CH_2), 19.02 (CH_3), 14.34 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{20}H_{26}NO_5$ 360.1811, found 360.1806.

Ethyl [(1*R,3*S**)-10-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1s):**

Reaction of the vinylogous carbonate **2a** (20 mg, 0.073 mmol) with TMSOTf (20 μL, 0.110 mmol) and naphthaquinone (22 mg, 0.146 mmol) in dry CH_2Cl_2 (6 mL) for 11 h, as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1s** (21 mg, 68 %) as a dark brown solid.



Physical appearance: dark brown solid

m.p.: 182-184 ^{o}C.

R_f: 0.3 (1:4, EtOAc:Hexanes).

IR (neat): 2980, 1736, 1657, 1588, 1462, 1370, 1293, 1243, 1169, 1093, 1034, 787 cm^{-1}.

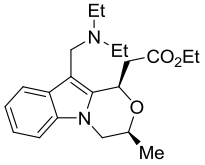
^{1}H NMR (400MHz, $CDCl_3$): δ 8.25-8.20 (m, 2H), 7.90-7.75 (m, 2H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.39 (d, *J* = 7.9 Hz, 1H), 7.35-7.20 (m, 3H), 5.86 (dd, *J* = 8.1, 2.7 Hz, 1H), 4.35-4.25 (m, 1H), 4.22 (ABX, *J* = 11.1, 2.8 Hz, 1H), 4.15-4.05 (m, 2H), 3.86 (ABX, *J* = 11.1, 11.0 H, 1H), 2.77 (ABX, *J* =15.9, 2.8 Hz, 1H), 2.66 (ABX, *J* = 15.9, 8.2 Hz, 1H), 1.53 (d, *J* = 6.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 185.18 (C), 184.82 (C), 169.88 (C), 143.85 (C), 136.70 (C), 135.72 (C), 134.80 (CH), 134.10 (C), 133.68 (CH), 132.56 (CH), 132.48 (C), 127.24 (CH), 127.02 (C), 126.15 (CH), 122.50 (CH), 121.84 (CH), 119.06 (CH), 109.29 (CH), 103.03 (C), 71.71 (CH), 69.41 (CH), 60.70 (CH_2), 47.99 (CH_2), 41.12 (CH_2), 19.04 (CH_3), 14.16 (CH_3).

HRMS (ESI, M+H^{+}): m/z calcd. for $C_{26}H_{24}NO_5$ 430.1654, found 430.1649.

Ethyl [(1*R,3*S**)-10-((diethylamino)methyl)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1t):**

Reaction of the vinylogous carbonate **2a** (55 mg, 0.201 mmol) with TMSOTf (55 μL, 0.305 mmol) and preformed iminium salt **9** [prepared by mixing 40% aq formalin (20 μL, 0.302 mmol), diethylamine (30 μL, 0.302 mmol) and AcOH (0.1 mL) in EtOH (2 mL)] in dry CH_2Cl_2 (6 mL) for 12 h, as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1t** (38 mg, 77 %) as a hygroscopic solid.



Physical appearance: hygroscopic solid

R_f: 0.3 (1:4, EtOAc:Hexanes).

IR (neat): 2971, 2880, 1733, 1461, 1372, 1284, 1247, 1163, 1094, 1051, 962, 916, 734 cm^{-1}.

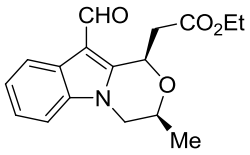
^{1}H NMR (400MHz, $CDCl_3$): δ 7.52 (d, *J* = 7.7 Hz, 1H), 7.20-7.10 (m, 1H), 7.07 (dt, *J* = 7.2, 0.6 Hz, 1H), 7.02 (dt, *J* = 8.0, 1.1 Hz, 1H), 5.38 (dd, *J* = 9.2, 2.0 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.97 (ABX, *J* = 11.3, 2.8 Hz, 1H), 3.95-3.80 (m, 1H), 3.72 (ABX, *J* = 15.9, 2.4 Hz, 1H), 3.70-3.50 (m, 3H), 2.73 (ABX, *J* = 15.9, 9.3 Hz, 1H), 2.39 (q, *J* = 7.1 Hz, 4H), 1.31 (d, *J* = 6.1 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 6H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 171.38 (C), 135.08 (C), 132.25 (C), 129.05 (C), 121.03 (CH), 119.67 (CH), 118.71 (CH), 108.50 (CH), 106.56 (C), 71.70 (CH), 69.88 (CH), 60.43 (CH_2), 47.99 (CH_2), 47.91 (CH_2), 46.38 (2C, CH_2), 40.40 (CH_2), 19.05 (CH_3), 14.37 (CH_3), 11.73 (2C, CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{21}H_{31}N_2O_3$ 359.2335, found 359.2335.

Ethyl [(1*R,3*S**)-10-formyl-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetate (1u):**

Reaction of the vinylogous carbonate **2a** (25 mg, 0.091 mmol) with TMSOTf (35 μL, 0.183 mmol) and triethylorthoformate (45 μL, 0.274 mmol) in dry CH_2Cl_2 (6 mL) for 30 min., as described for the oxazinoindole **1m** followed by purification on a silica gel column using ethyl acetate-hexanes (1:9) as eluent furnished the oxazinoindole **1n** (26 mg, 95 %) as a hygroscopic solid.



Physical appearance: hygroscopic solid

R_f: 0.5 (1:4, EtOAc:Hexanes).

IR (neat): 2980, 1734, 1649, 1514, 1464, 1364, 1287, 1242, 1178, 1096, 1039, 751 cm^{-1}.

^{1}H NMR (400MHz, $CDCl_3$): δ 10.24 (s, 1H), 8.08 (dd, *J* = 5.0, 2.5 Hz, 1H), 7.40-7.25 (m, 3H), 5.71 (dd, *J* = 6.8, 3.2 Hz, 1H), 4.20-4.10 (m, 3H), 4.05-3.95 (m, 1H), 3.83 (ABX, *J* = 11.4, 10.6 Hz, 1H), 3.39 (ABX, *J* = 16.4, 3.3 Hz, 1H), 3.14 (ABX, *J* = 16.4, 6.9 Hz, 1H), 1.45 (d, *J* = 6.1 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H).

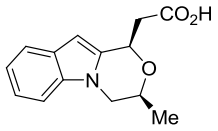
^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 183.40 (C), 170.31 (C), 143.47 (C), 135.74 (C), 127.35 (C), 123.42 (CH), 123.23 (CH), 119.28 (CH), 111.07 (C), 109.56 (CH), 71.15 (CH), 69.33 (CH), 60.72 (CH_2), 47.91 (CH_2), 40.30 (CH_2), 18.78 (CH_3), 14.25 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{17}H_{20}NO_4$ 302.1392, found 302.1397.

2-[(1*R,3*S**)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]acetic acid (11a):**

To a stirred solution of the oxazinoindole **1a** (88 mg, 0.32 mmol) in EtOH (5 mL) was added 10% aq. NaOH (5 mL) and stirred overnight at r.t. After completion of the reaction, the solvent was evaporated and the reaction mixture was acidified to pH 2 using 2N HCl and then extracted with ethyl acetate (3 x 5 mL), washed with brine and dried (anhyd. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel

column using ethyl acetate-hexanes (2:1) as the eluent furnished the acid **11a** (69 mg, 87%) as a syrupy liquid.



Physical appearance: syrupy liquid

R_f: 0.5 (3:1, EtOAc:Hexanes).

IR (neat): 3049, 2977, 2874, 1710, 1456, 1416, 1355, 1310, 1154, 1090, 1038, 955, 782, 738 cm^{-1}.

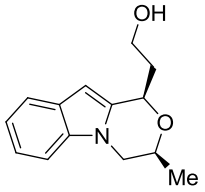
^{1}H NMR (400MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.7 Hz, 1H), 7.28 (d, *J* = 8.0 Hz, 1H), 7.21 (dt, *J* = 7.7, 0.8 Hz, 1H), 7.13 (dt, *J* = 8.0, 0.8 Hz, 1H), 6.25 (s, 1H), 5.37 (dd, *J* = 8.6, 3.9 Hz, 1H), 4.25-4.15 (m, 1H), 4.13 (ABX, *J* = 11.0, 3.2 Hz, 1H), 3.67 (ABX, *J* = 11.0, 11.0 Hz, 1H), 3.12 (ABX, *J* = 16.2, 3.9 Hz, 1H), 2.94 (ABX, *J* = 16.2, 8.6 Hz, 1H), 1.47 (d, *J* = 6.1 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 175.79 (C), 136.18 (C), 134.91 (C), 128.05 (C), 121.61 (CH), 120.69 (CH), 120.39 (CH), 108.89 (CH), 96.01 (CH), 71.01 (CH), 70.64 (CH), 47.82 (CH_2), 40.12 (CH_2), 19.23 (CH_3).

HRMS (ESI, M+H^+): m/z calcd. for $C_{14}H_{16}NO_3$ 246.1130, found 246.1126.

2-[(1*R,3*S**)-3-methyl-3,4-dihydro-1*H*-[1,4]oxazino[4,3-*a*]indol-1-yl]ethanol (12a):**

To a magnetically stirred solution of the oxazino indole **1a** (300 mg, 1.097 mmol) in dry THF (5 mL) at 0 ^oC was added LAH (62 mg, 1.64 mmol) in portions and allowed to warm to r.t for 3 h. After completion of the reaction (TLC control), moist Na_2SO_4 was added and the reaction mass was filtered and the filtrate was dried (*anhyd*. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexanes (1:3) furnished the alcohol **15b** (210 mg, 83%) as a sticky solid which was then recrystallized from hexanes and ether.



Physical appearance: white solid

R_f: 0.3 (1:3, EtOAc:Hexanes).

mp: 94-96 ^oC.

IR (neat): 3380, 2875, 1457, 1362, 1318, 1234, 1151, 1095, 1054, 781, 743 cm^{-1}.

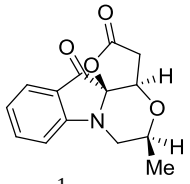
^{1}H NMR (400MHz, $CDCl_3$): δ 7.58 (d, *J* = 7.7 Hz, 1H), 7.27 (d, *J* = 9.2 Hz, 1H), 7.19 (dt, *J* = 7.7, 0.8 Hz, 1H), 7.12 (dt, *J* = 7.7, 0.8 Hz, 1H), 6.22 (s, 3H), 5.15 (dd, *J* = 8.0, 2.9 Hz, 1H), 4.20-4.10 (m, 2H), 3.93 (t, *J* = 5.7 Hz, 2H), 3.67 (ABX, *J* = 11.8, 11.7 Hz, 1H), 2.45-2.30 (m, 1H), 2.25-2.10 (m, 1H), 1.46 (d, *J* = 6.0 Hz, 3H).

^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 136.15 (C), 135.98 (C), 128.18 (C), 121.38 (CH), 120.59 (CH), 120.29 (CH), 108.80 (CH), 95.88 (CH), 74.66 (CH), 70.62 (CH), 60.74 (CH_2), 47.89 (CH_2), 36.76 (CH_2), 19.38 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{14}H_{18}NO_2$ 232.1338, found 232.1338.

(3*aR,5*S**,12*aR**)-5-methyl-3,3*a*,5,6-tetrahydro-2*H*,12*H*-furo[3',2':2,3][1,4]oxazino[4,3-*a*]indole-2,12-dione (13a):**

To a stirred solution of the acid **11a** (28 mg, 0.114 mmol) in dry CH_2Cl_2 (6 mL) at r.t., was added *m*-CPBA (50 mg, 0.290 mmol.) and stirred until completion of the reaction (1 h, TLC control). The reaction mixture was then quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2 (3 x 10 mL), washed with brine and dried (*anhyd*. Na_2SO_4). Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexanes (1:19) gave the spirooxoindole **13a** (22 mg, 76%) as a brown syrupy liquid.



Physical appearance: brown syrupy liquid

R_f: 0.5 (1:19, EtOAc:Hexanes).

IR (neat): 2924, 2854, 1738, 1621, 1470, 1374, 1263, 1154, 1026, 878, 749 cm^{-1}.

^{1}H NMR (400MHz, C_6D_6): δ 7.42 (d, *J* = 7.5 Hz, 1H), 7.00 (td, *J* = 8.3, 1.2 Hz, 1H), 6.41 (t, *J* = 7.5 Hz, 1H), 6.14 (d, *J* = 8.3 Hz, 1H), 3.39 (d, *J* = 5.0 Hz, 1H), 3.09 (dd, *J* = 4.9, 4.8 Hz, 1H), 2.79 (d, *J* = 11.2 Hz, 1H), 2.75-2.60 (m, 2H), 2.40 (d, *J* = 17.2 Hz, 1H), 0.71 (d, *J* = 5.5 Hz, 3H).

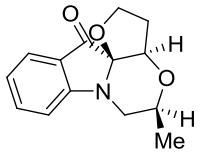
^{13}C NMR (100MHz, C_6D_6, DEPT): δ 195.00 (C), 172.71 (C), 159.32 (C), 138.37 (CH), 125.76 (CH), 119.88 (C), 119.07 (CH), 109.82 (CH), 90.63 (C), 73.09 (CH), 69.46 (CH), 46.45 (CH_2), 36.84 (CH_2), 17.74 (CH_3).

HRMS (ESI, M+H$^+$): m/z calcd. for $C_{14}H_{14}NO_4$ 260.0923, found 260.0921.

(3*aR,5*S**,12*aR**)-5-methyl-3,3*a*,5,6-tetrahydro-2*H*,12*H*-furo[3',2':2,3][1,4]oxazino[4,3-*a*]indole-12-one (14a):**

To a stirred solution of the alcohol **12a** (33 mg, 0.142 mmol) in dry CH_2Cl_2 (6 mL) at r.t., was added *m*-CPBA (75 mg, 0.428 mmol.) and stirred until completion of the reaction (1 h, TLC control). The reaction mixture was then quenched with saturated $NaHCO_3$, extracted with CH_2Cl_2 (3 x 10 mL), washed with brine and dried (*anhyd*. Na_2SO_4).

Evaporation of the solvent and purification of the residue on a silica gel column using ethyl acetate-hexanes (1:19) and recrystallisation of the residue obtained, from ethyl acetate-hexanes gave the spirooxoindole **14a** (24 mg, 69%) as a brown solid.



Physical appearance: brown solid

R_f: 0.5 (1:19, EtOAc:Hexanes).

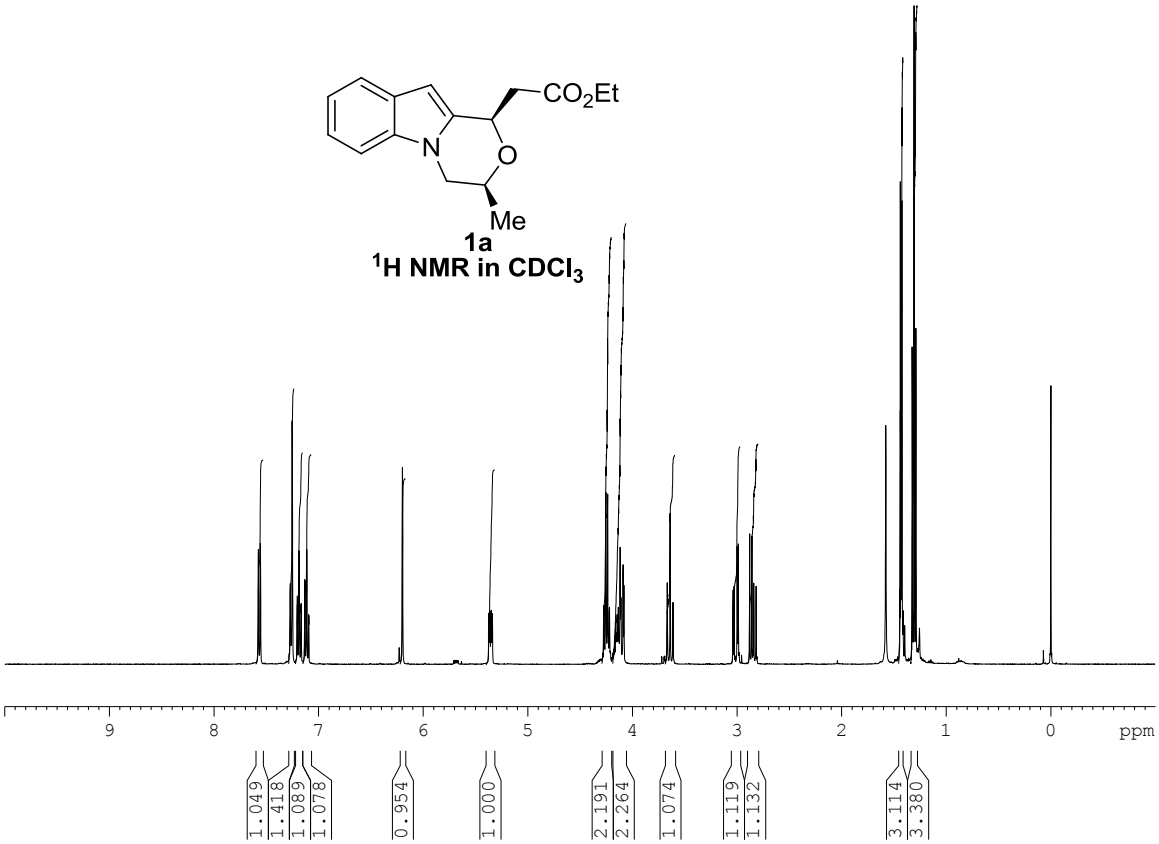
mp: 166-168 ^{o}C

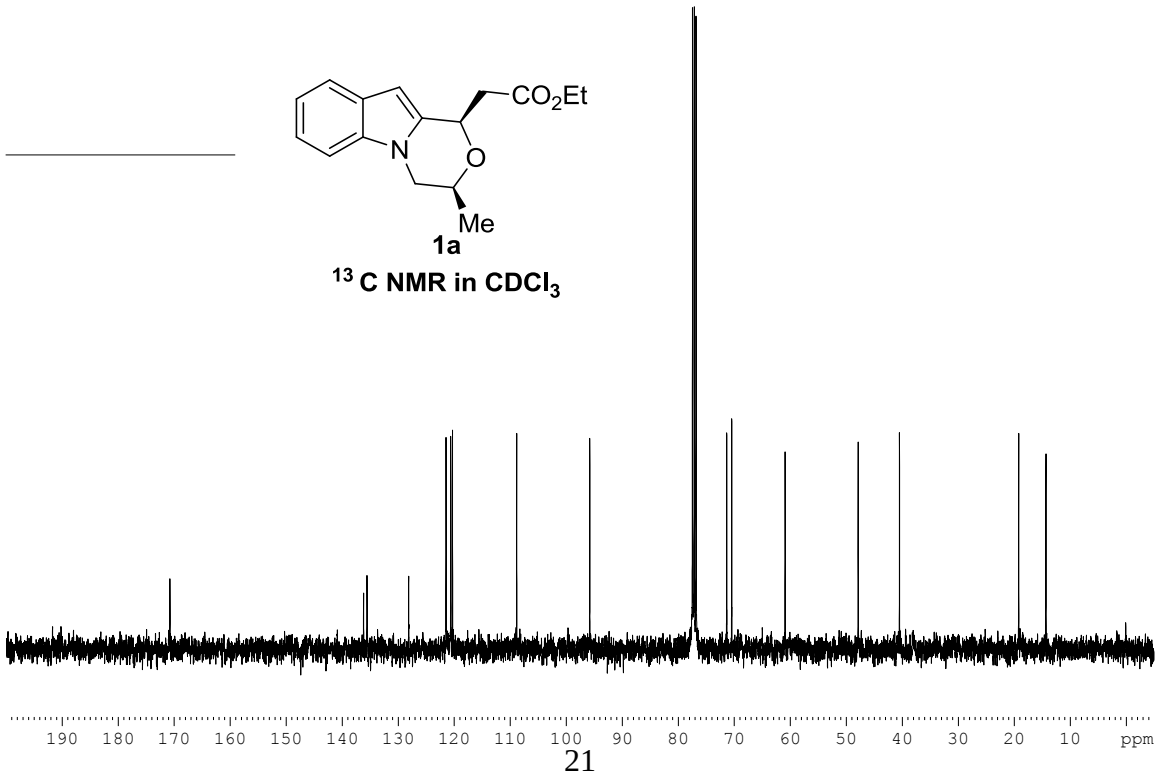
IR (neat): 2920, 1706, 1609, 1473, 1373, 1318, 1261, 1142, 1080, 1032, 934, 876, 755 cm^{-1}.

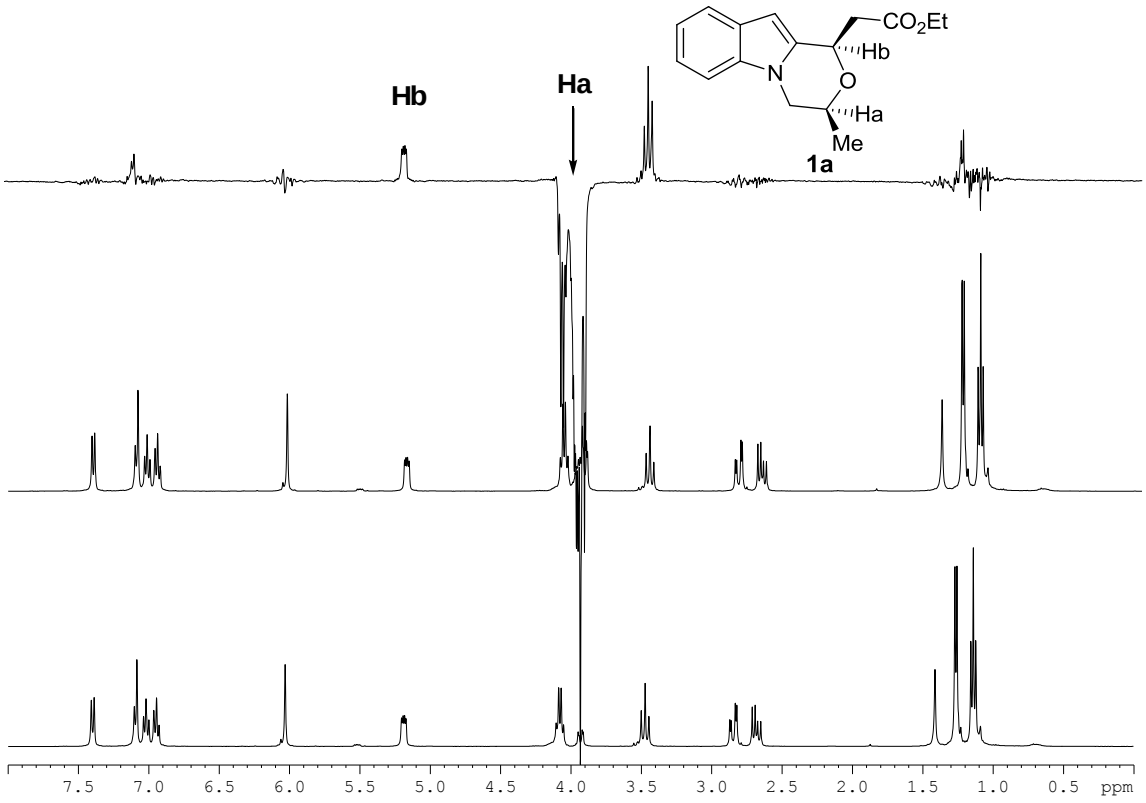
^{1}H NMR (400MHz, $CDCl_3$): δ 7.54 (d, *J* = 7.4 Hz, 1H), 7.47 (dt, *J* = 8.2, 1.0 Hz, 1H), 6.80-6.75 (m, 2H), 4.38 (dt, *J* = 10.5, 7.1 Hz, 1H), 4.29 (dt, *J* = 8.9, 1.2 Hz, 1H), 3.86 (d, *J* = 4.3 Hz, 1H), 3.52 (ABX, *J* = 13.6, 2.2 Hz, 1H), 3.50-3.40 (m, 1H), 3.15 (ABX, *J* = 13.6, 10.6 Hz, 1H), 2.75-2.65 (m, 1H), 2.12 (dd, *J* = 13.2, 5.6 Hz, 1H), 1.20 (d, *J* = 6.1 Hz, 3H).

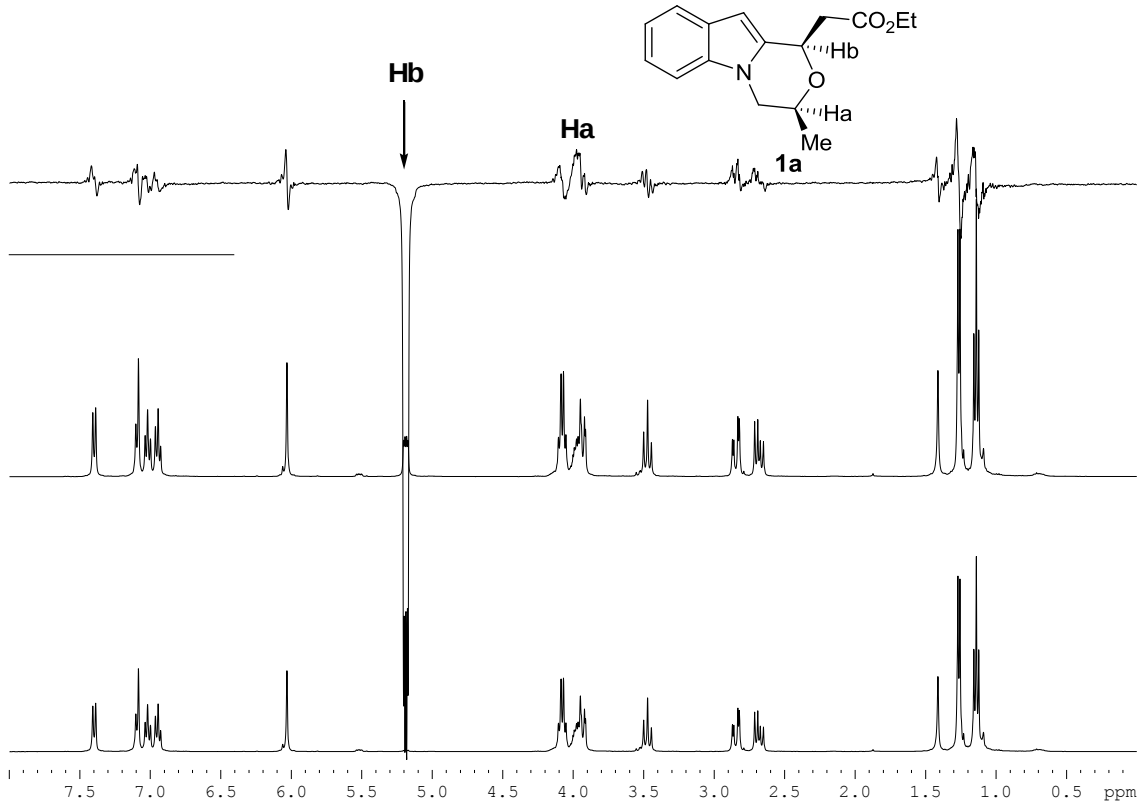
^{13}C NMR (100MHz, $CDCl_3$, DEPT): δ 199.73 (C), 159.33 (C), 138.06 (CH), 125.35 (CH), 119.58 (C), 118.90 (CH), 109.80 (CH), 93.99 (C), 75.13 (CH), 69.27 (CH), 68.14 (CH_2), 47.27 (CH_2), 31.64 (CH_2), 18.38 (CH_3).

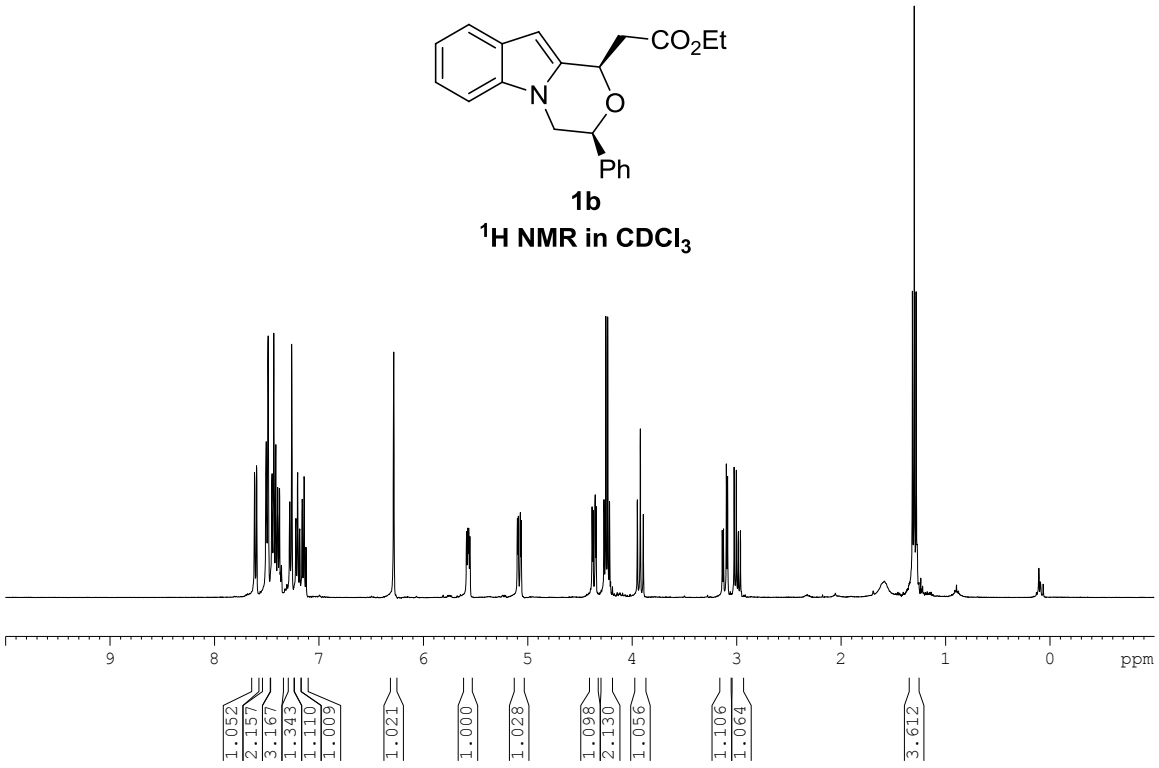
HRMS (ESI, M+H^+): m/z calcd. for $C_{14}H_{16}NO_3$ 246.1130, found 246.


CO2Et
N
O
Me
1a
1H NMR in CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
1.049
1.418
1.089
1.078
0.954
1.000
2.191
2.264
1.074
1.119
1.132
3.114
3.380


CO2Et
N
O
Me
1a
13 C NMR in CDCl3
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
ppm

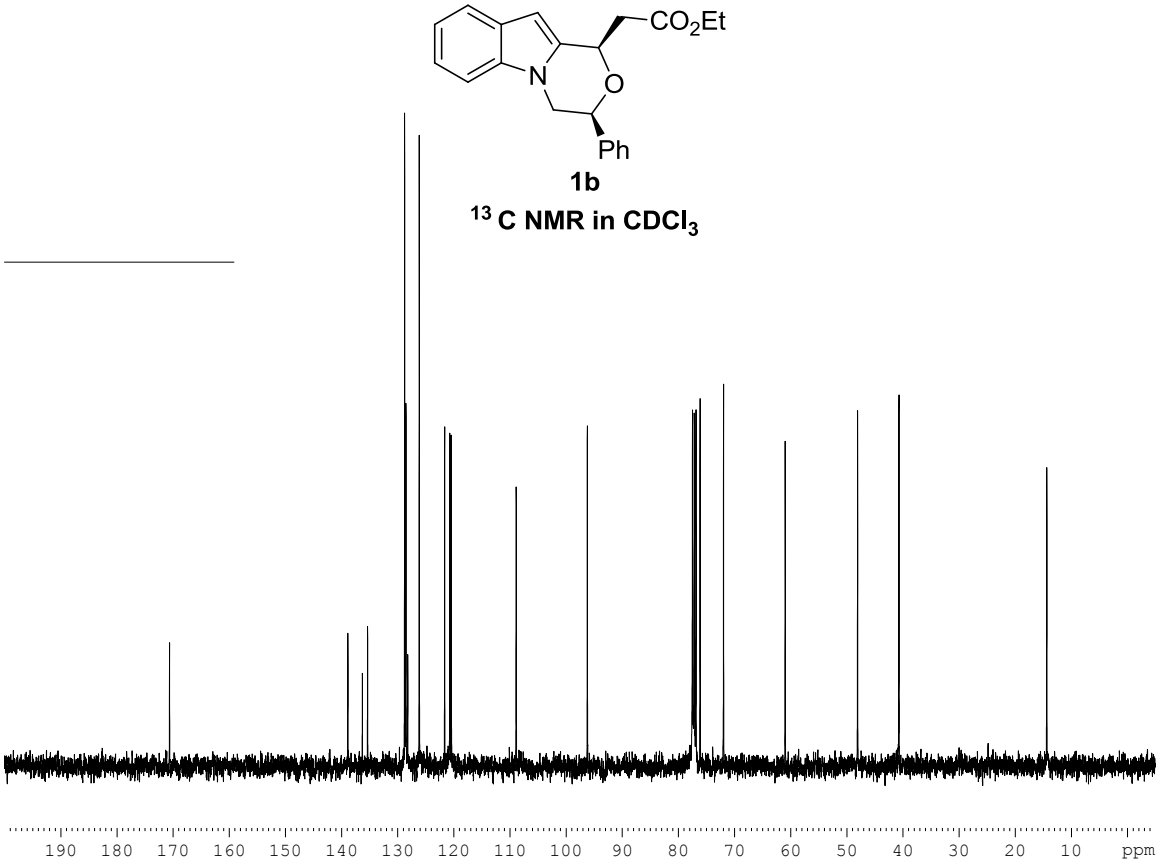

Hb
Ha
CO2Et
Hb
N
O
Ha
Me
1a
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Hb
Ha
CO2Et
Hb
N
O
Ha
Me
1a
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



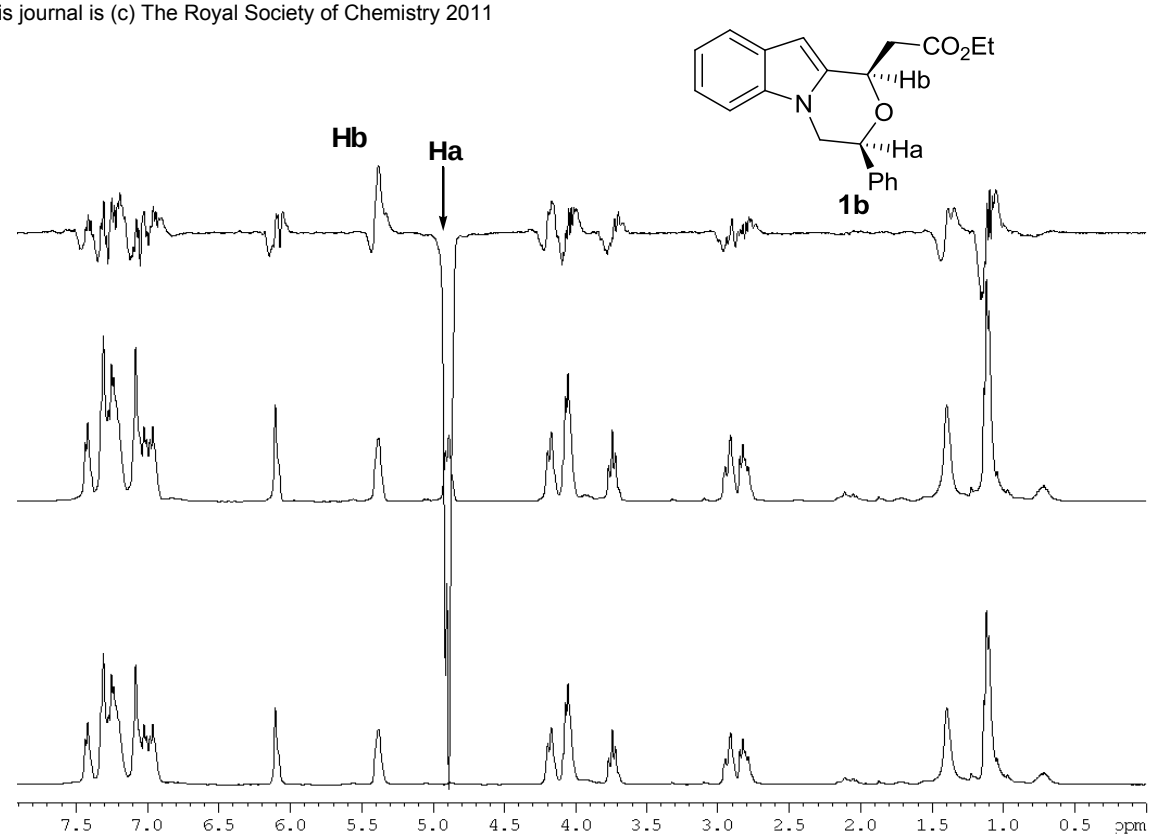
1b

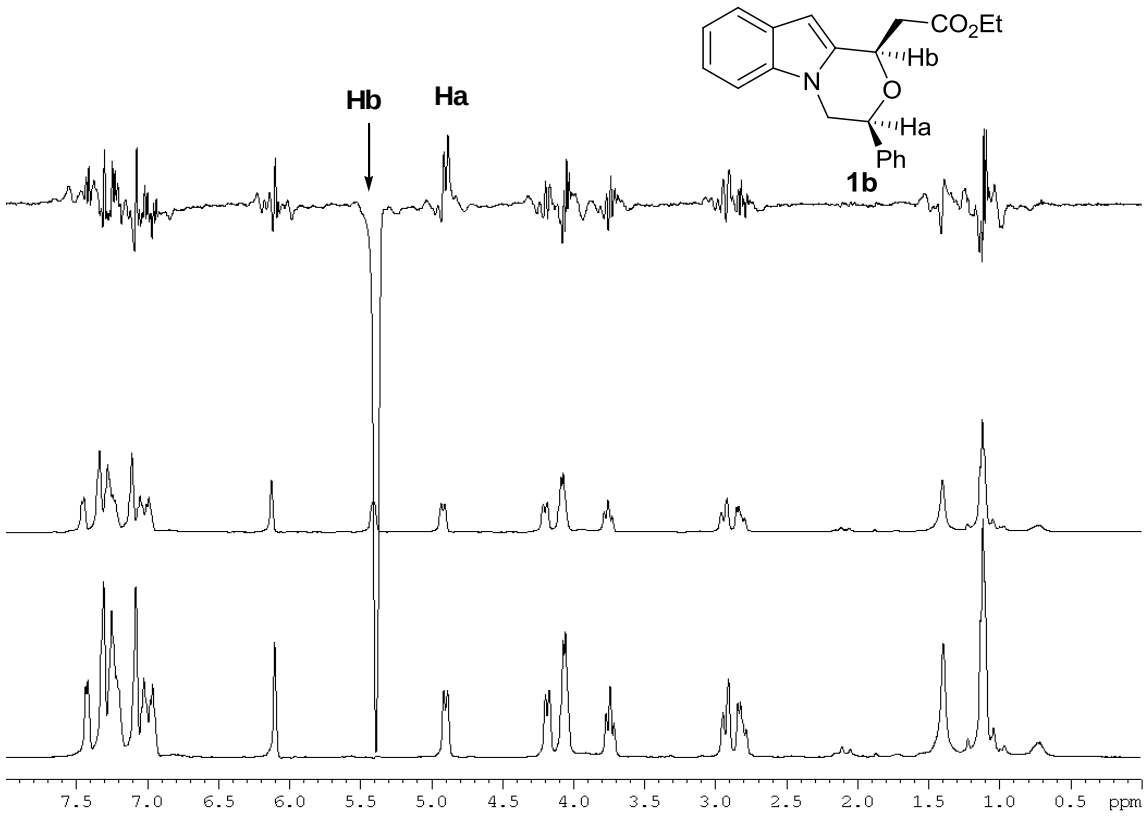
^{1}H NMR in $CDCl_3$

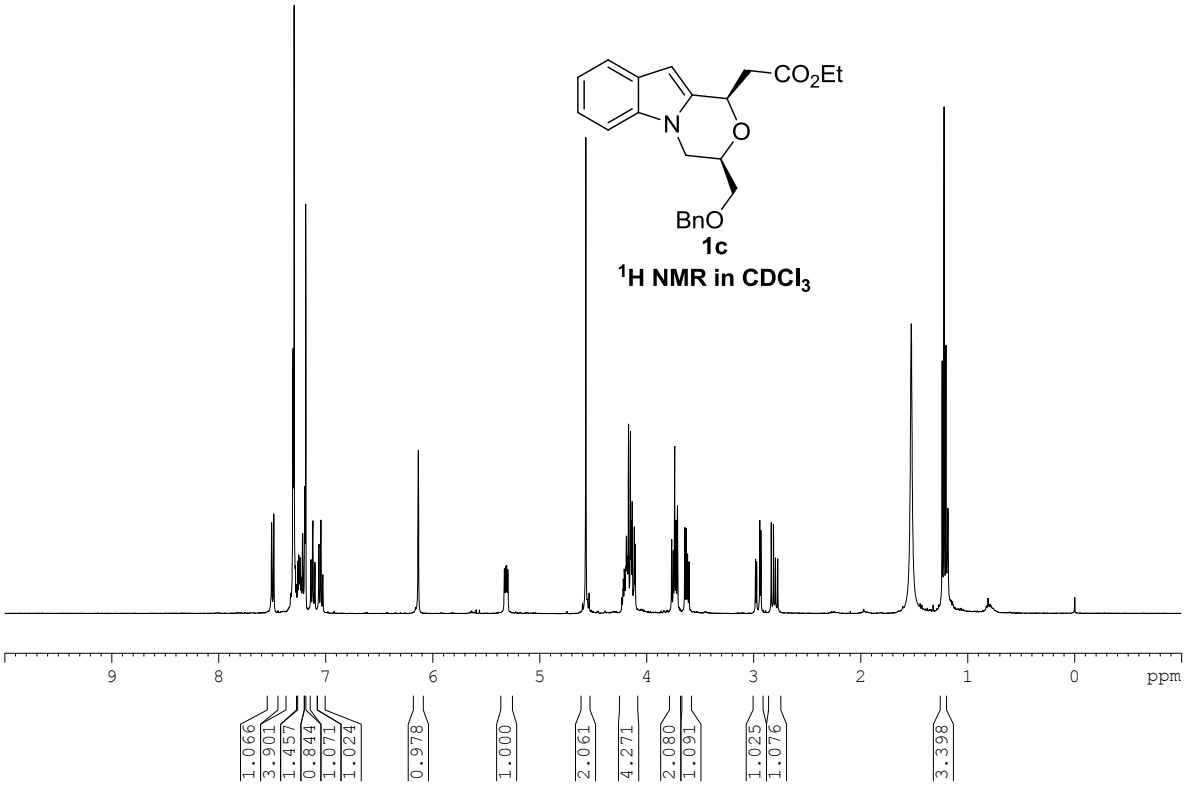


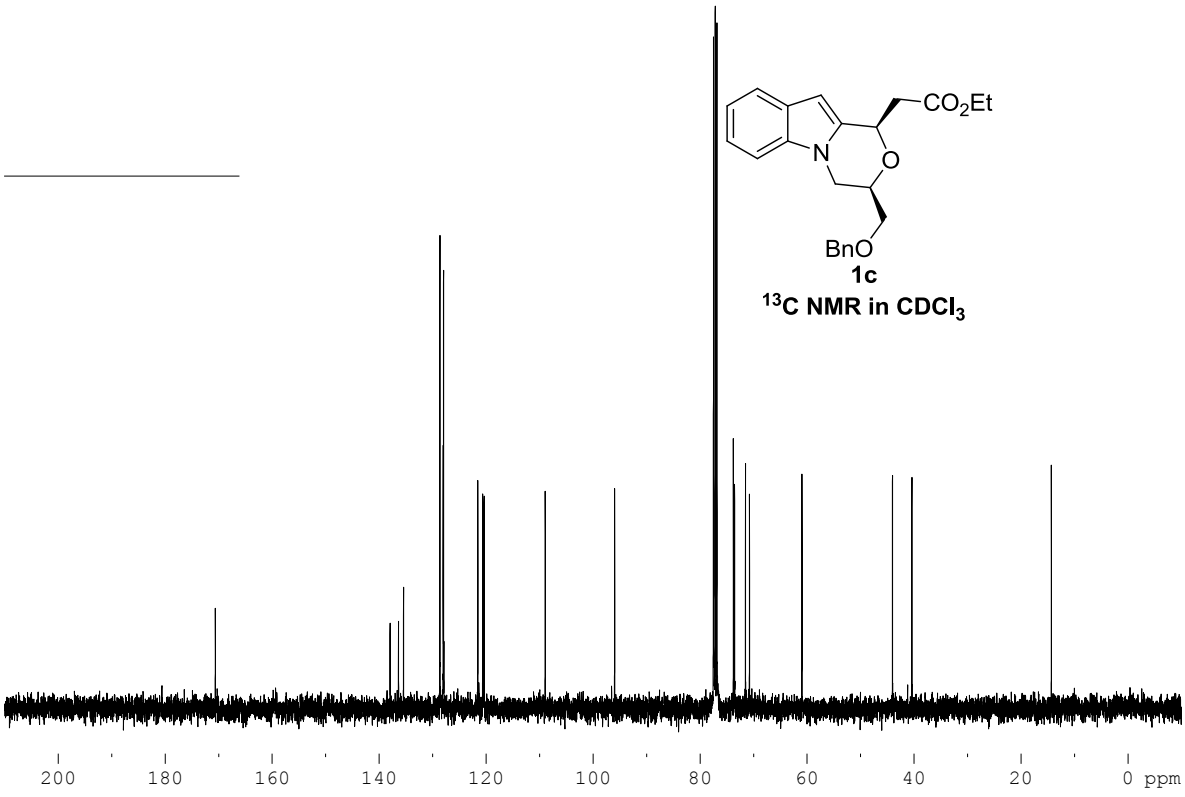
1b

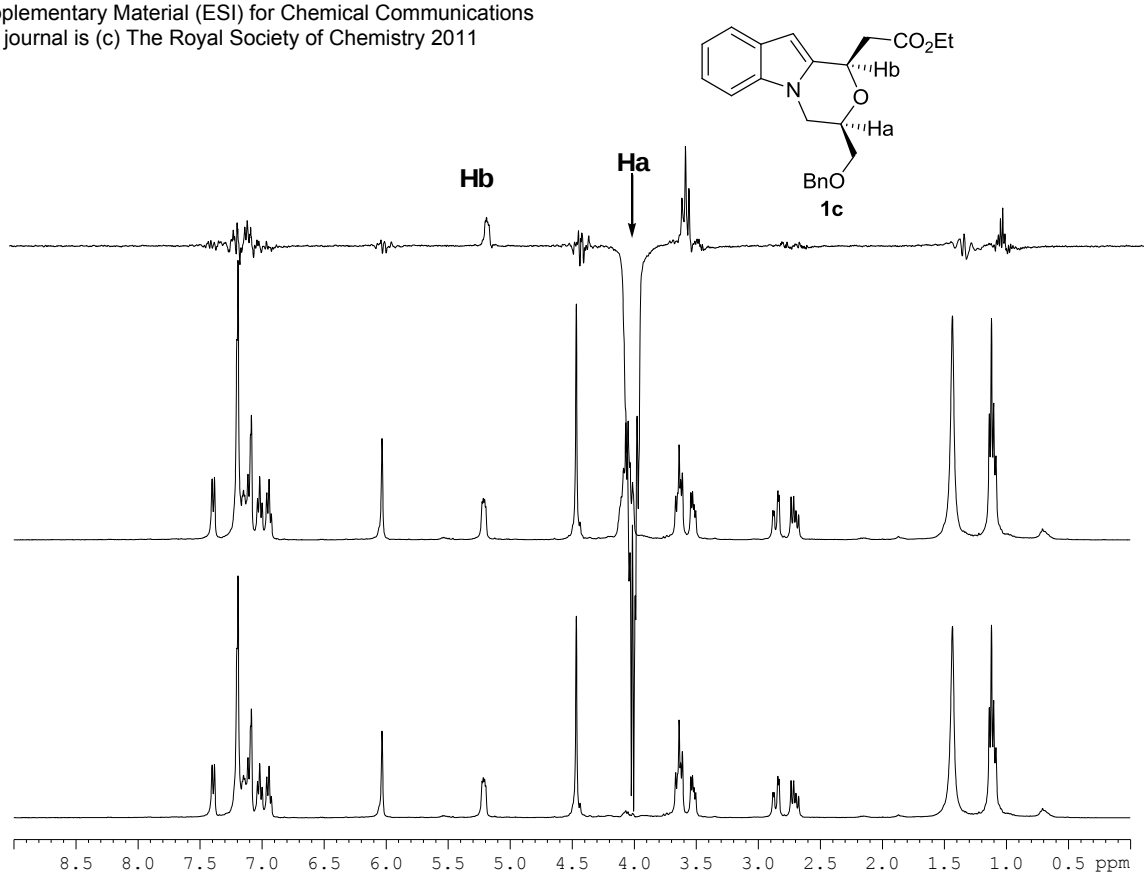
^{13}C NMR in $CDCl_3$

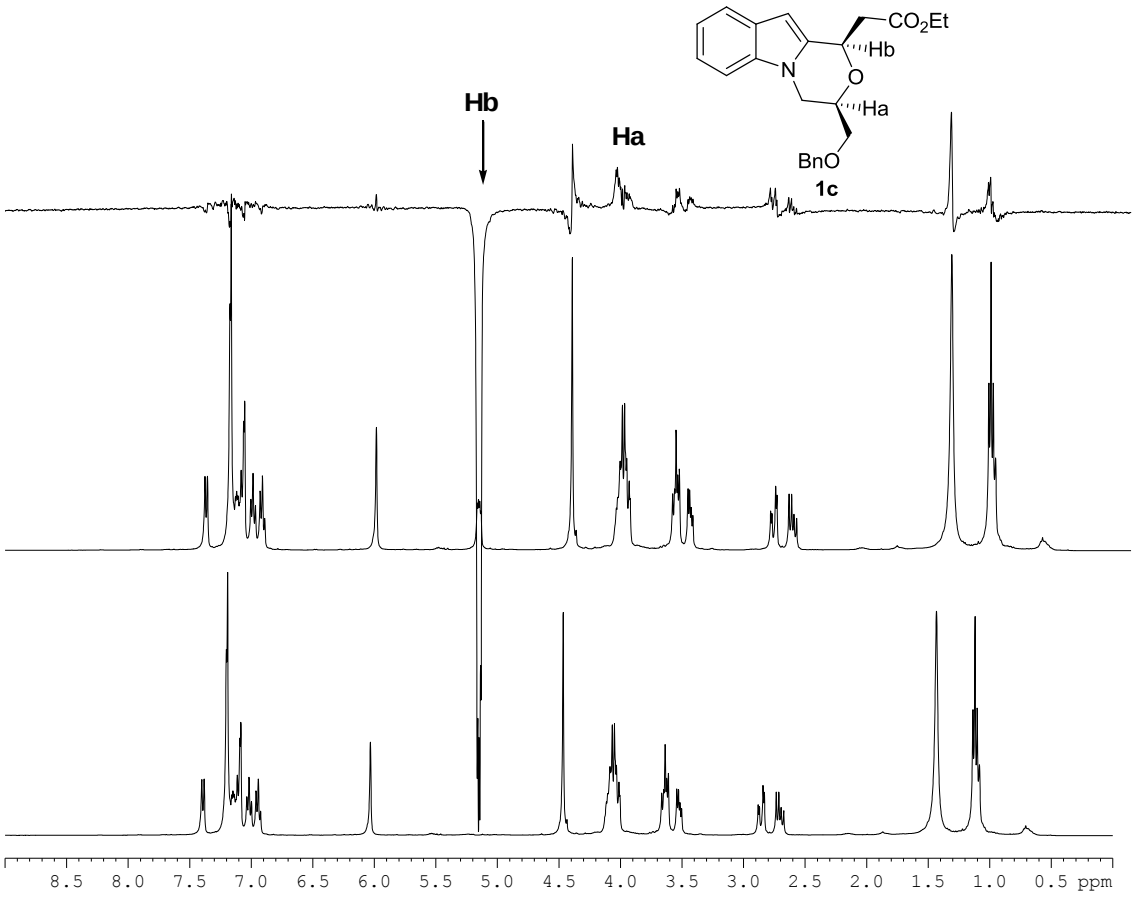

Hb
Ha
CO2Et
Hb
N
O
Ha
Ph
1b
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

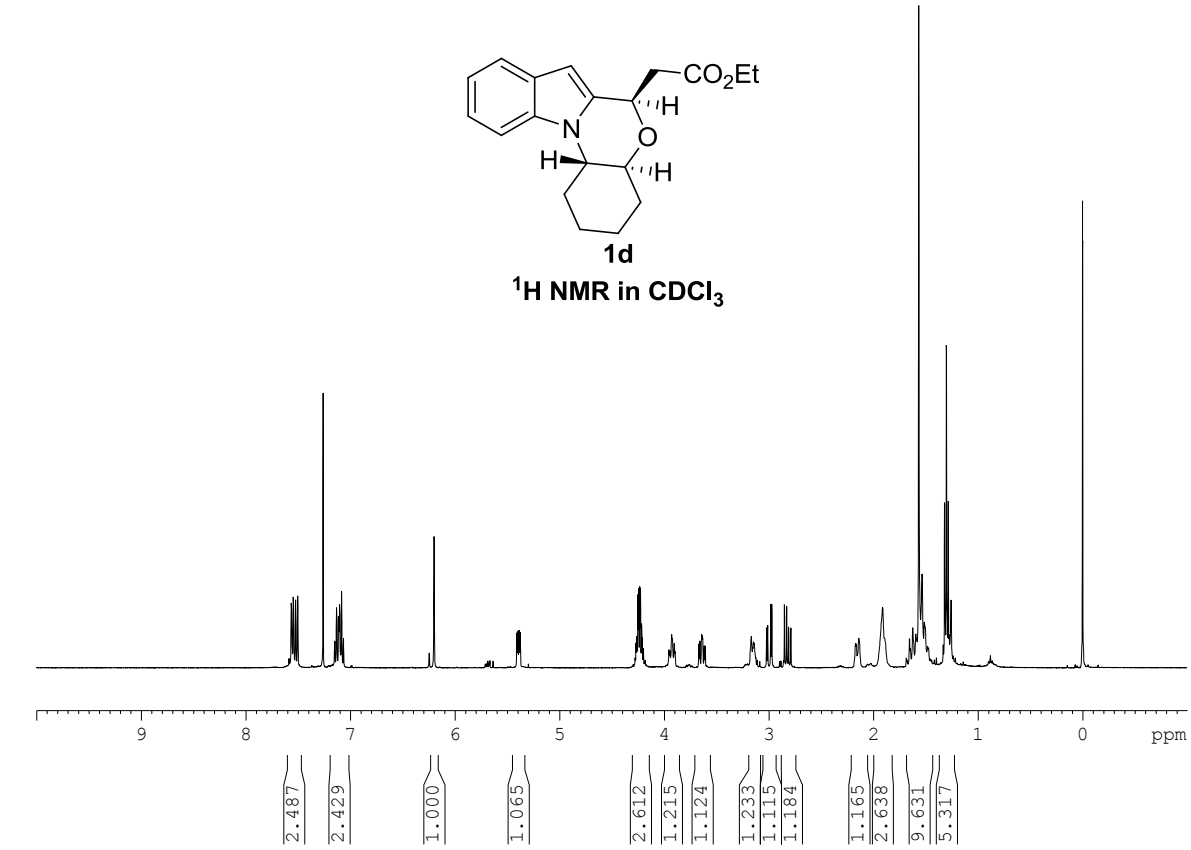

Hb
Ha
CO2Et
Hb
N
O
Ha
Ph
1b
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


CO2Et
N
O
BnO
1c
1H NMR in CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
1.066
3.901
1.457
0.844
1.071
1.024
0.978
1.000
2.061
4.271
2.080
1.091
1.025
1.076
3.398


CO2Et
N
O
BnO
1c
13C NMR in CDCl3
200
180
160
140
120
100
80
60
40
20
0 ppm

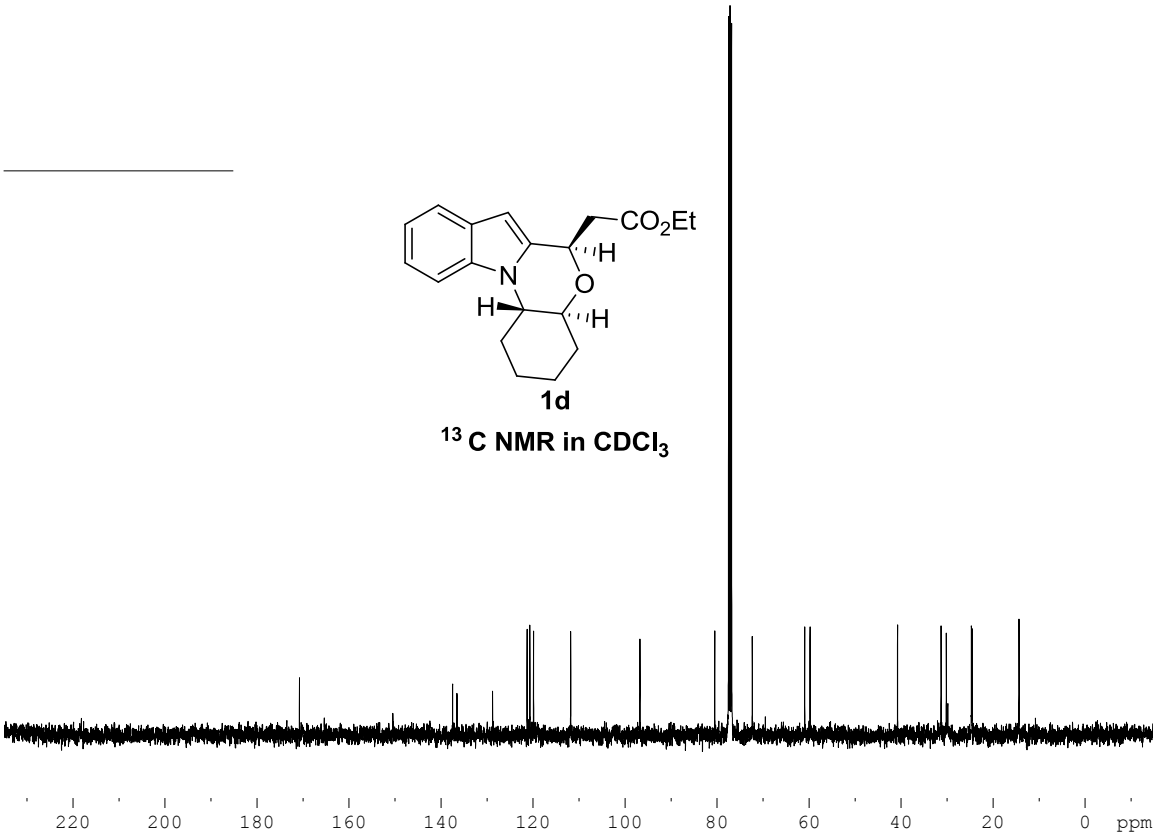

CO2Et
Hb
N
O
Ha
BnO
1c
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


CO2Et
Hb
N
O
Ha
BnO
1c
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



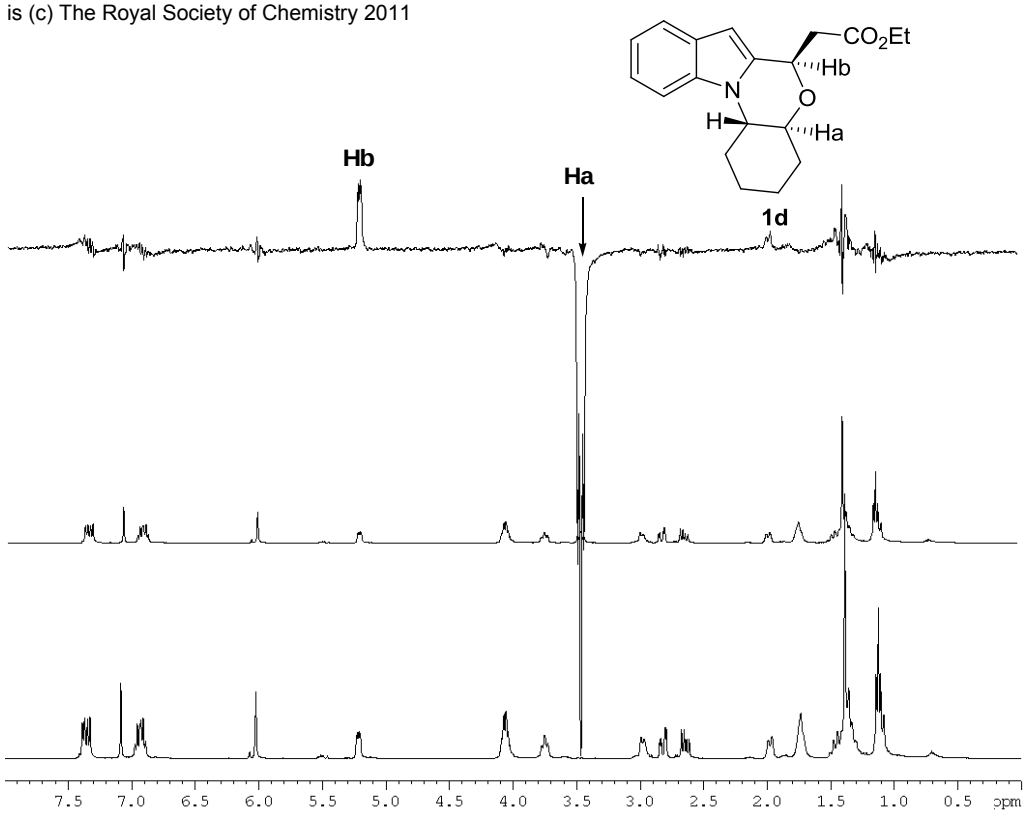
1d

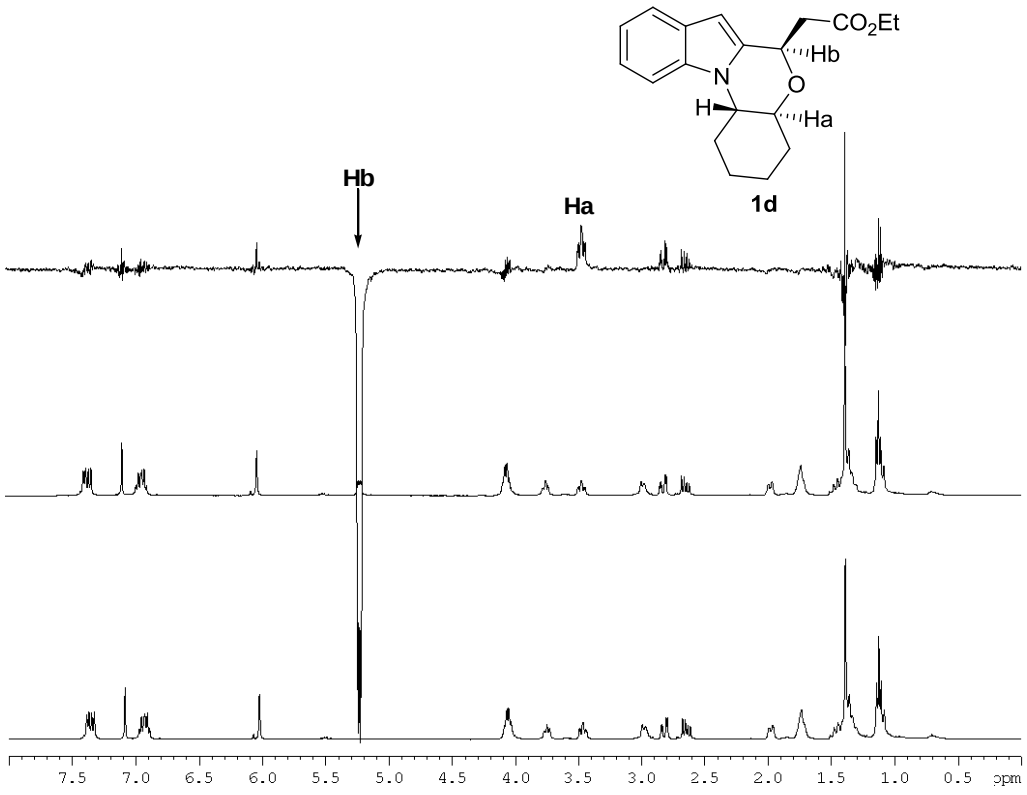
^{1}H NMR in $CDCl_3$

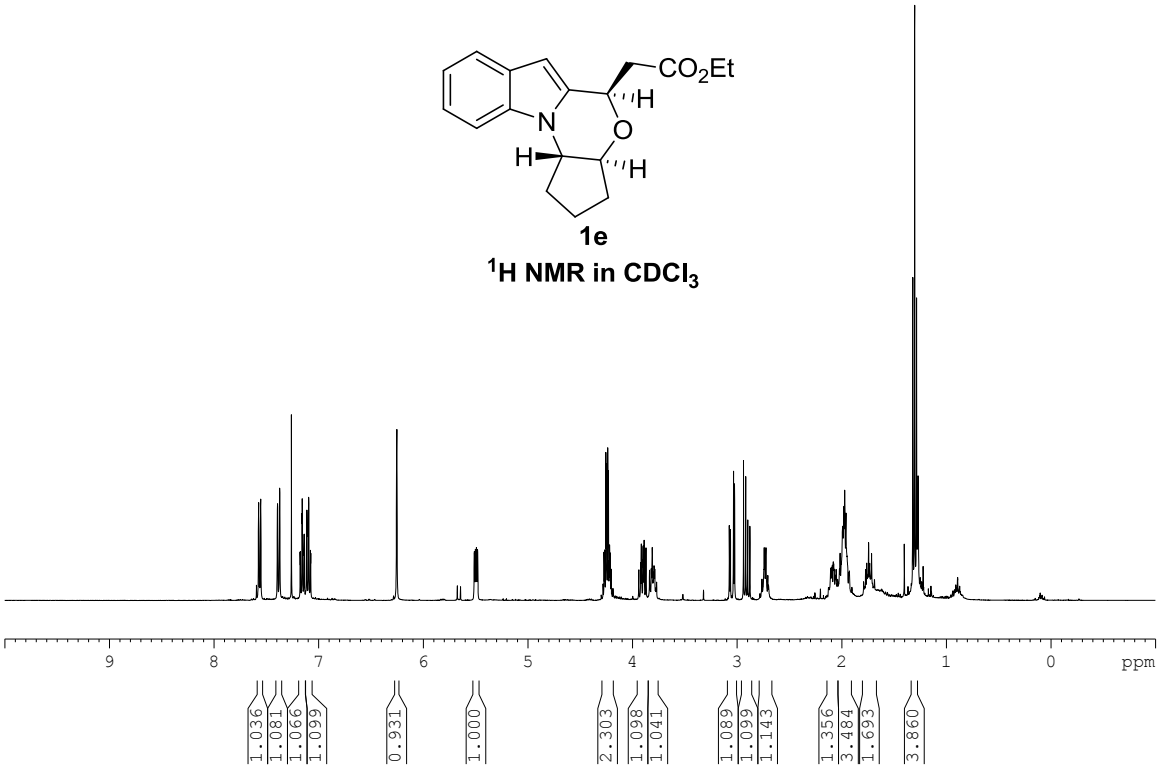


1d

^{13}C NMR in $CDCl_3$

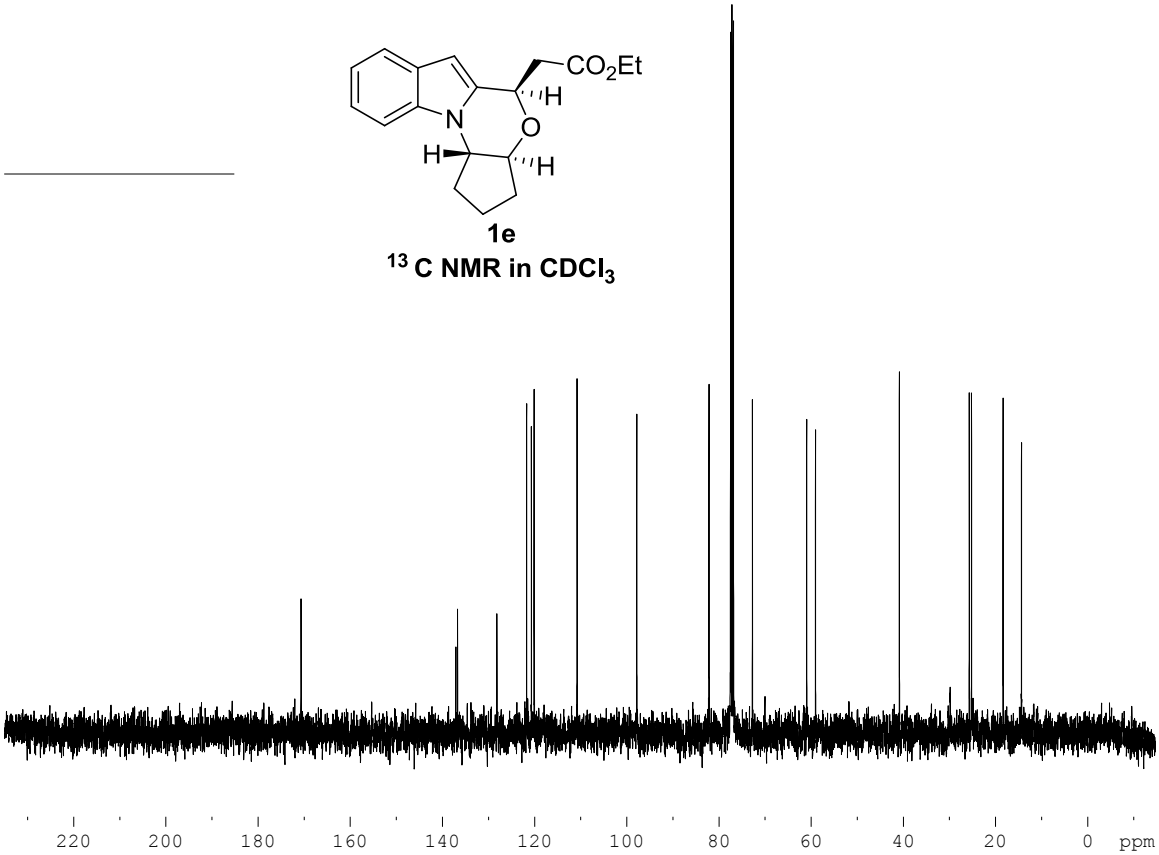

CO2Et
Hb
N
O
H
Ha
1d
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


CO2Et
Hb
N
O
H
Ha
1d
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



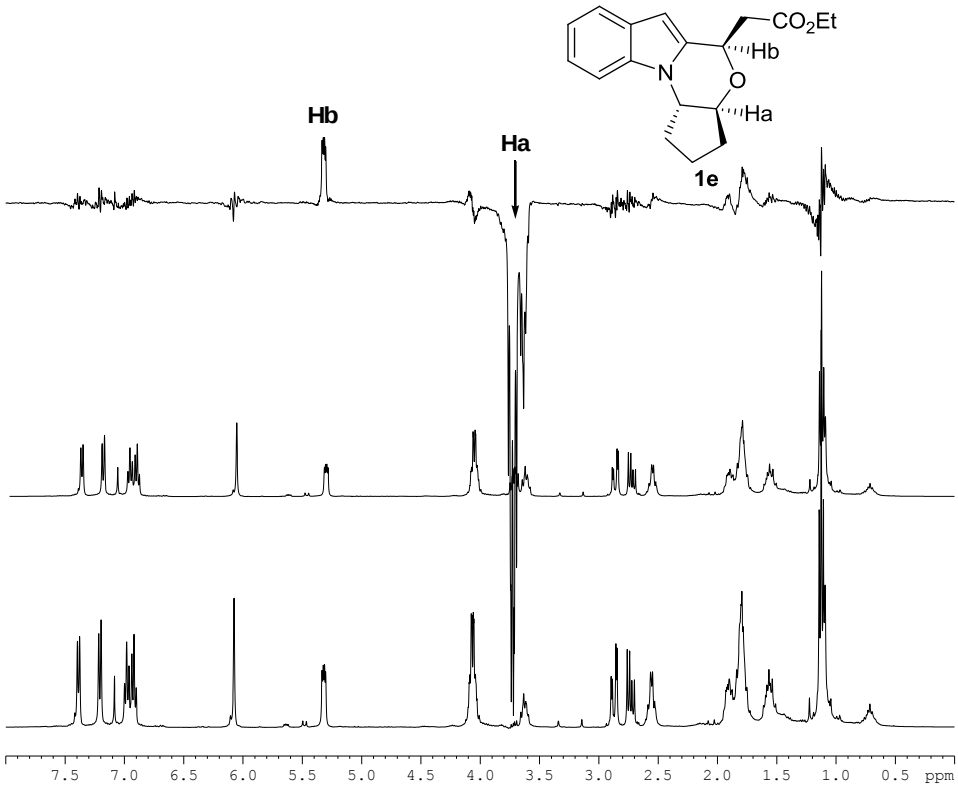
1e

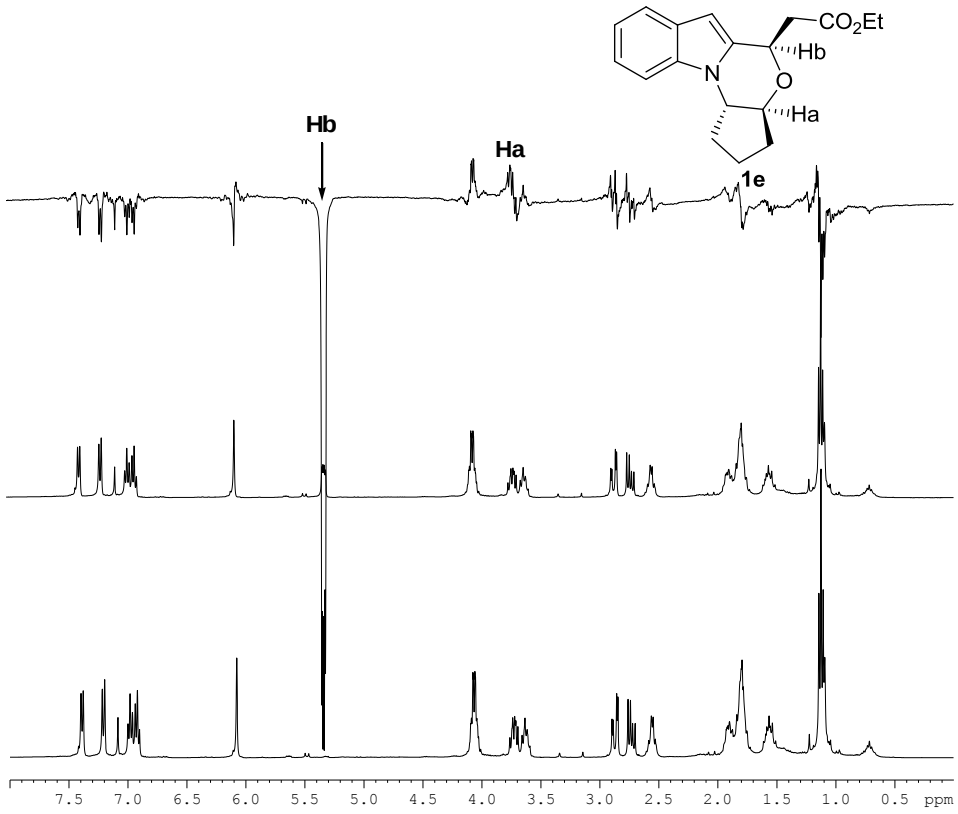
^{1}H NMR in $CDCl_3$

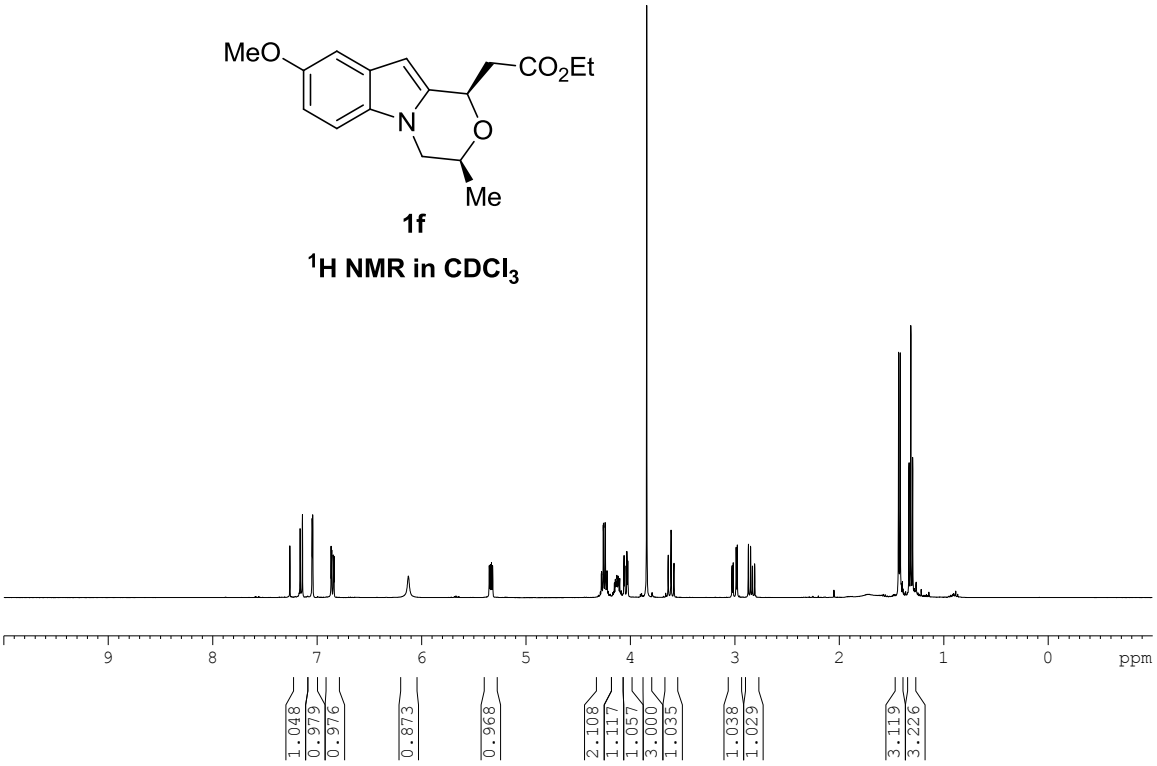


1e

^{13}C NMR in $CDCl_3$

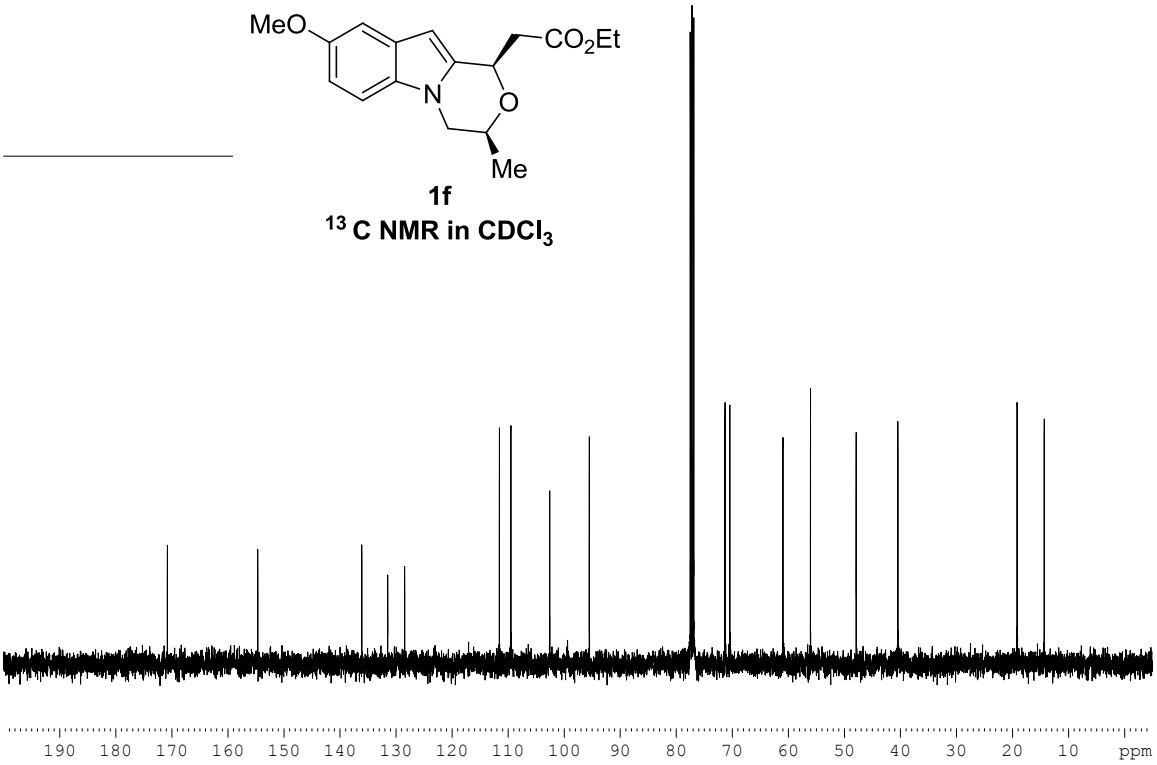

CO2Et
Hb
N
O
Ha
1e
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


CO2Et
Hb
N
O
Ha
1e
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



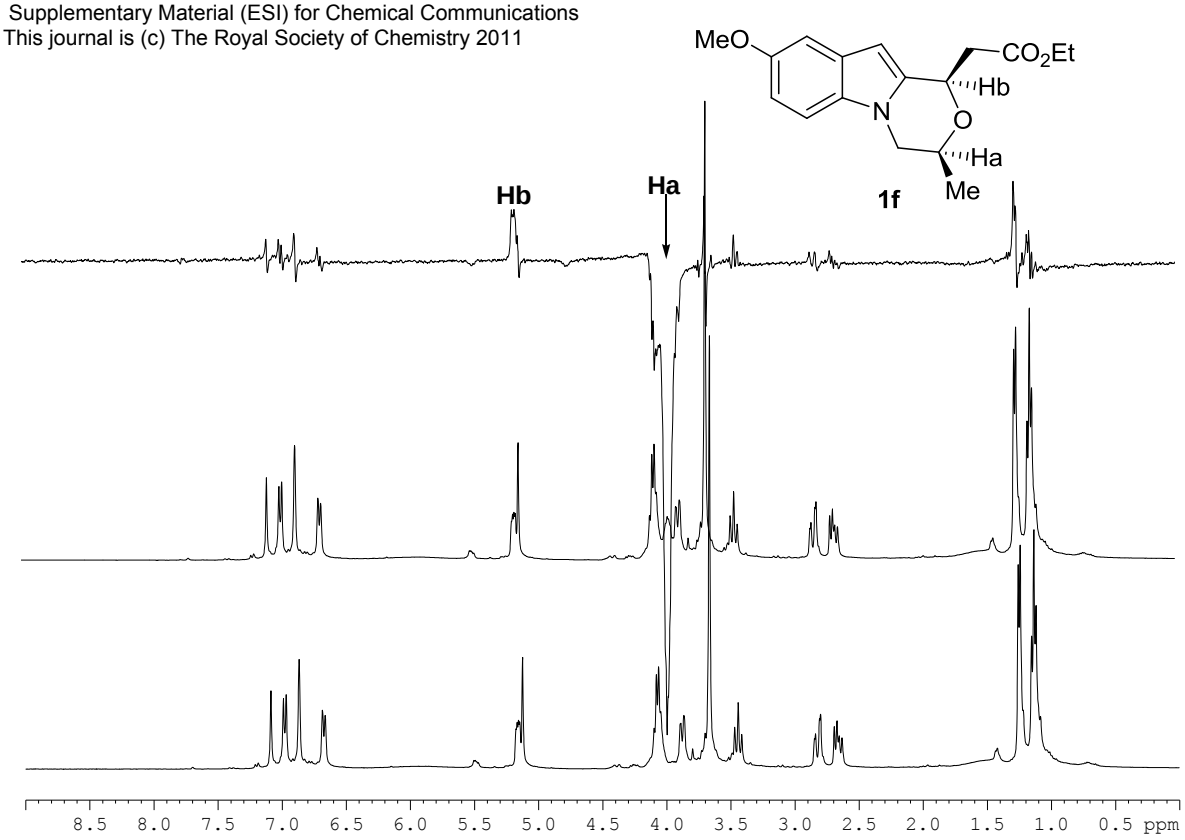
1f

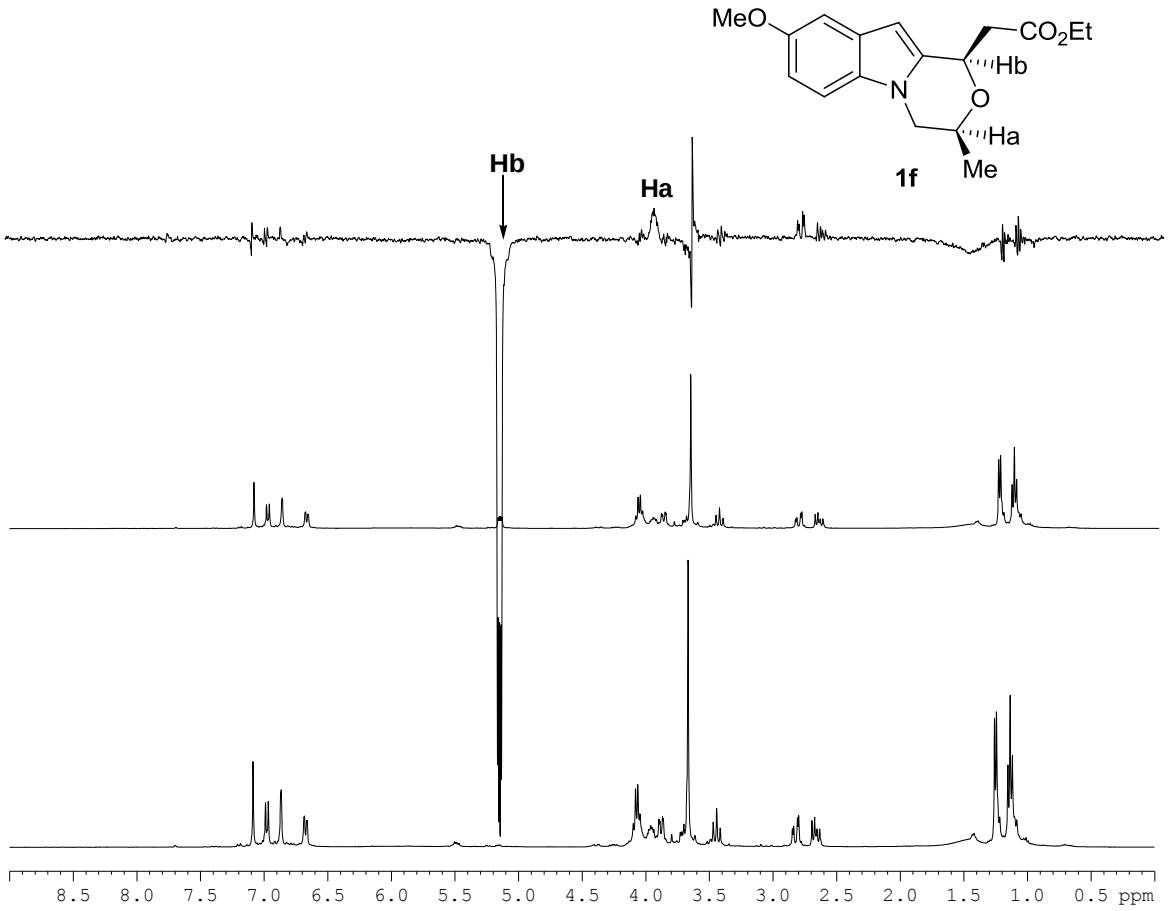
^{1}H NMR in $CDCl_3$

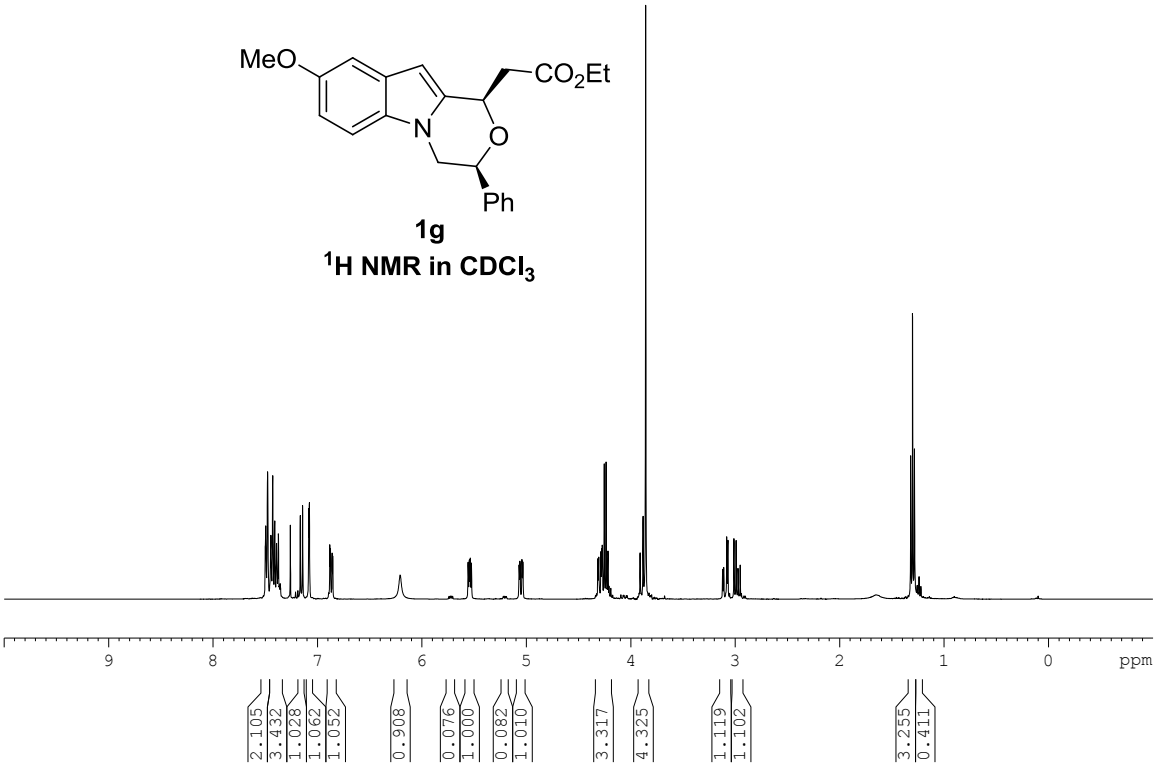


1f

^{13}C NMR in $CDCl_3$

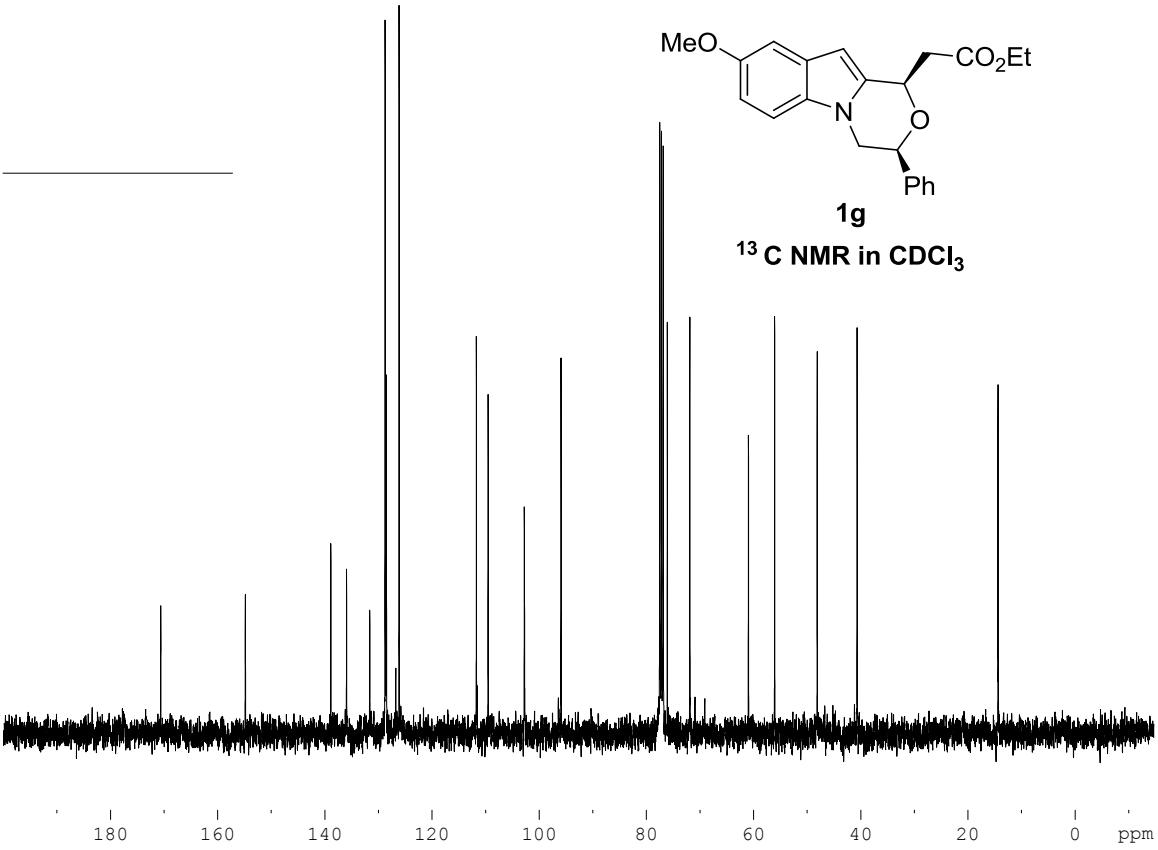

MeO
CO2Et
Hb
N
O
Ha
Me
1f
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


MeO
CO2Et
Hb
N
O
Ha
Me
1f
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



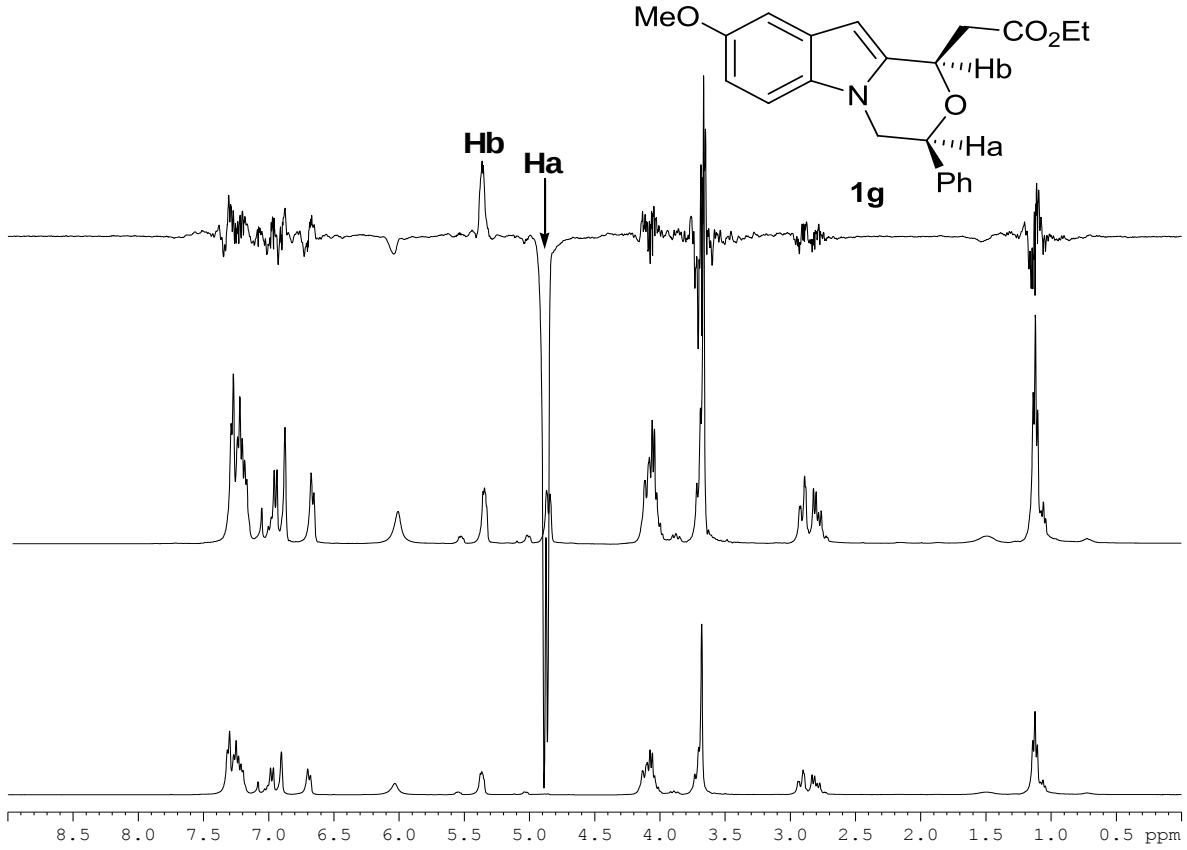
1g

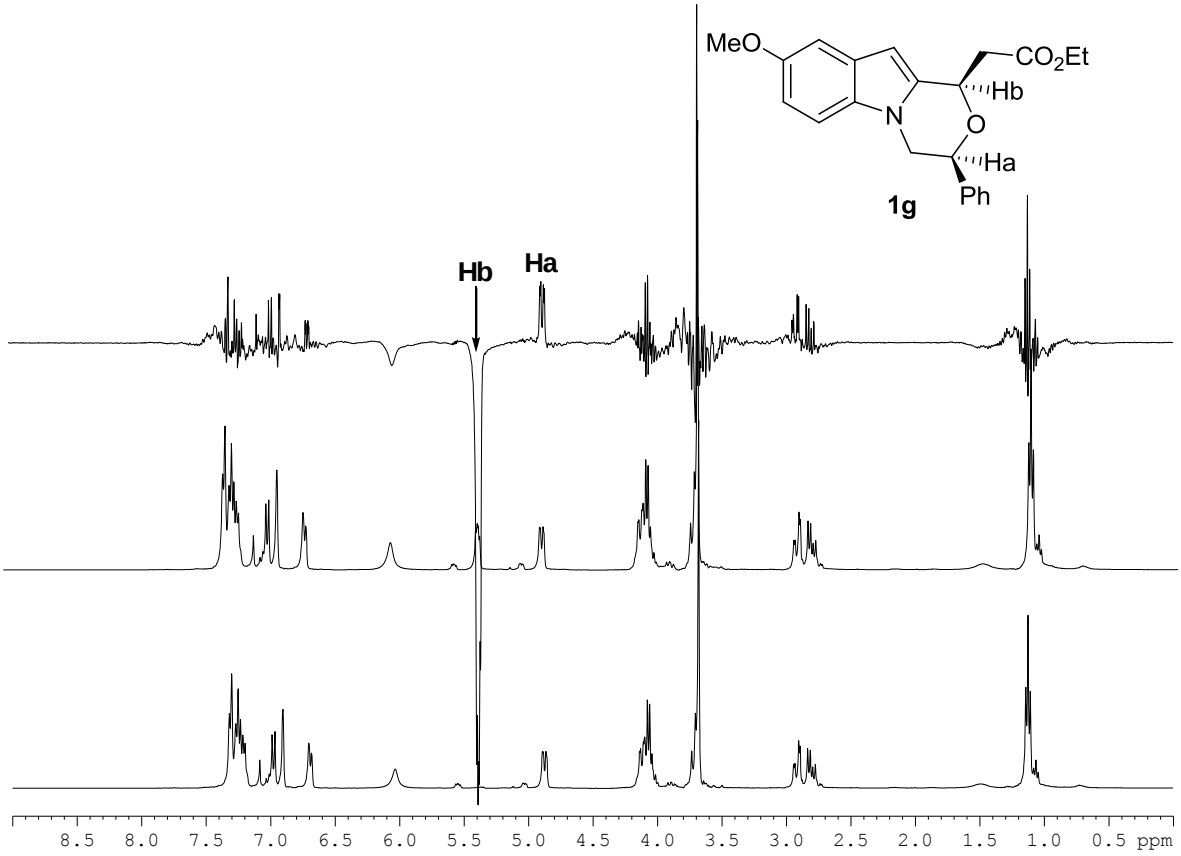
^{1}H NMR in $CDCl_3$

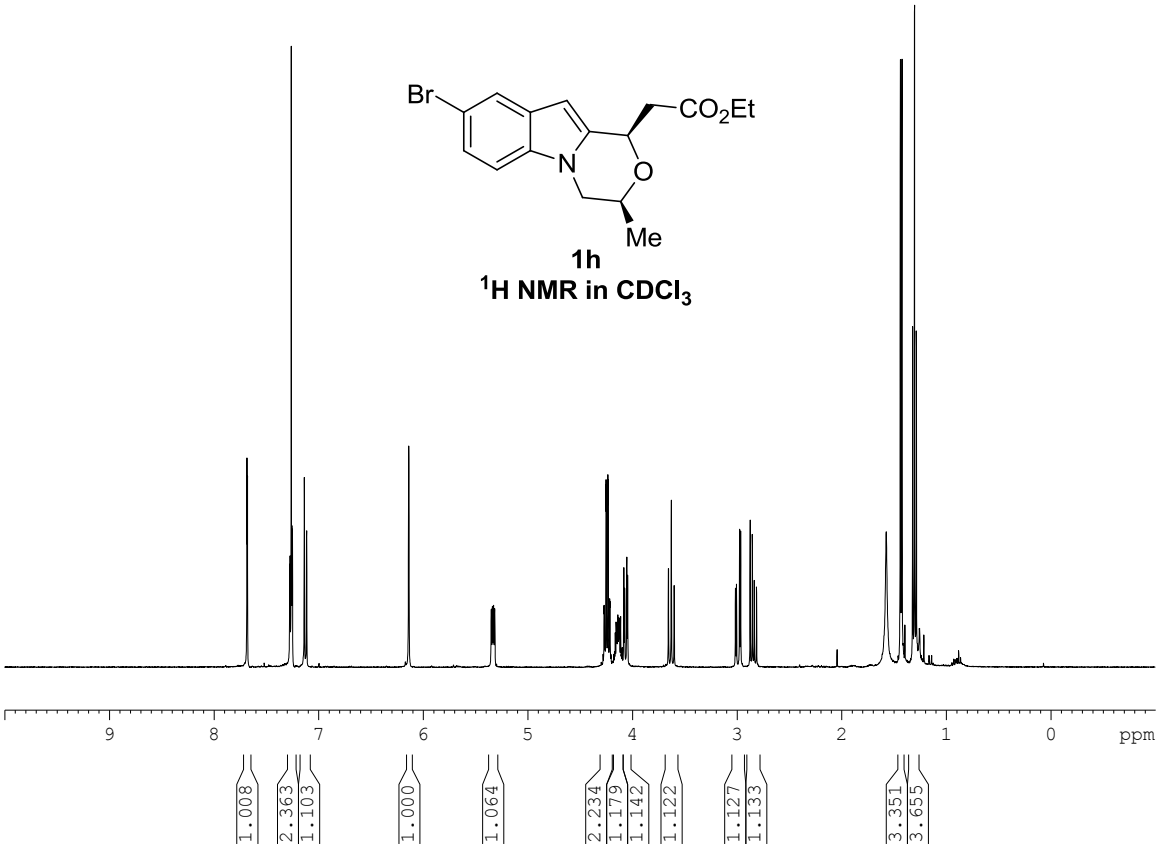


1g

^{13}C NMR in $CDCl_3$

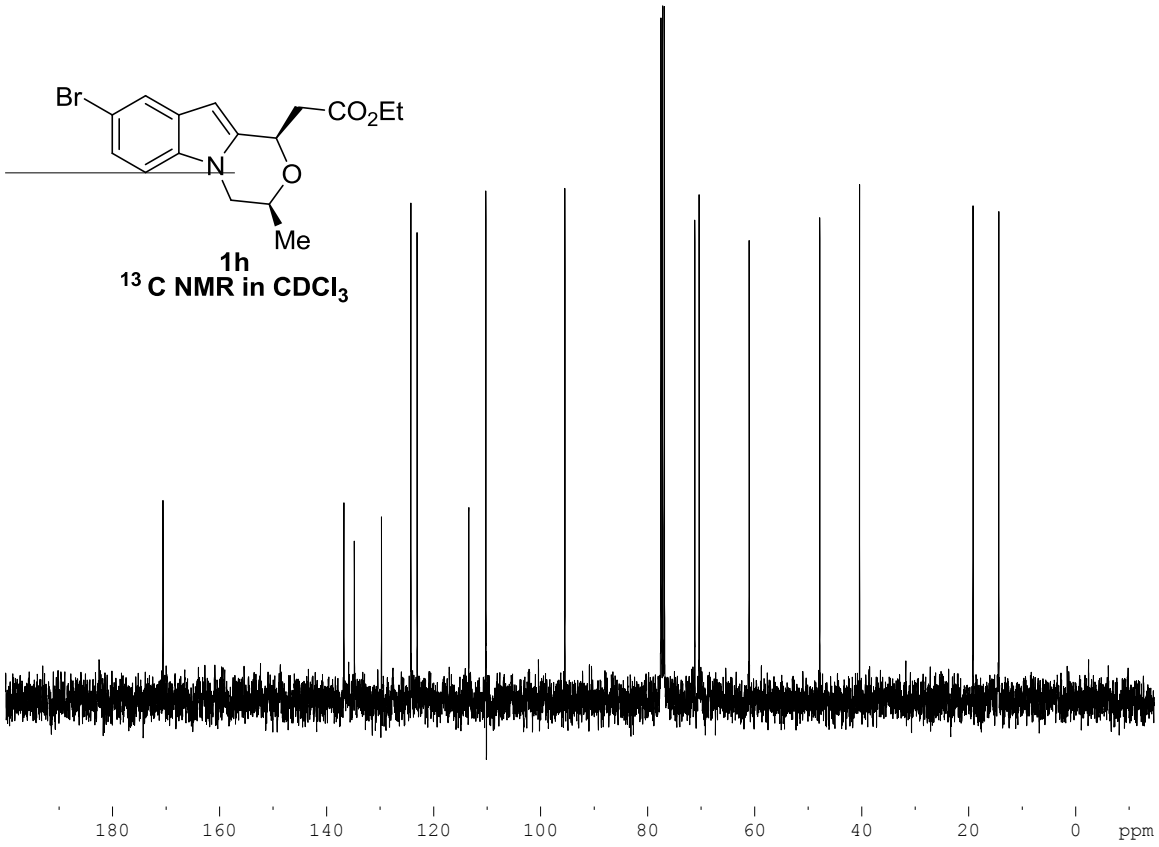

MeO
CO2Et
Hb
N
O
Ha
Ph
1g
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


MeO
CO2Et
Hb
N
O
Ha
Ph
1g
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



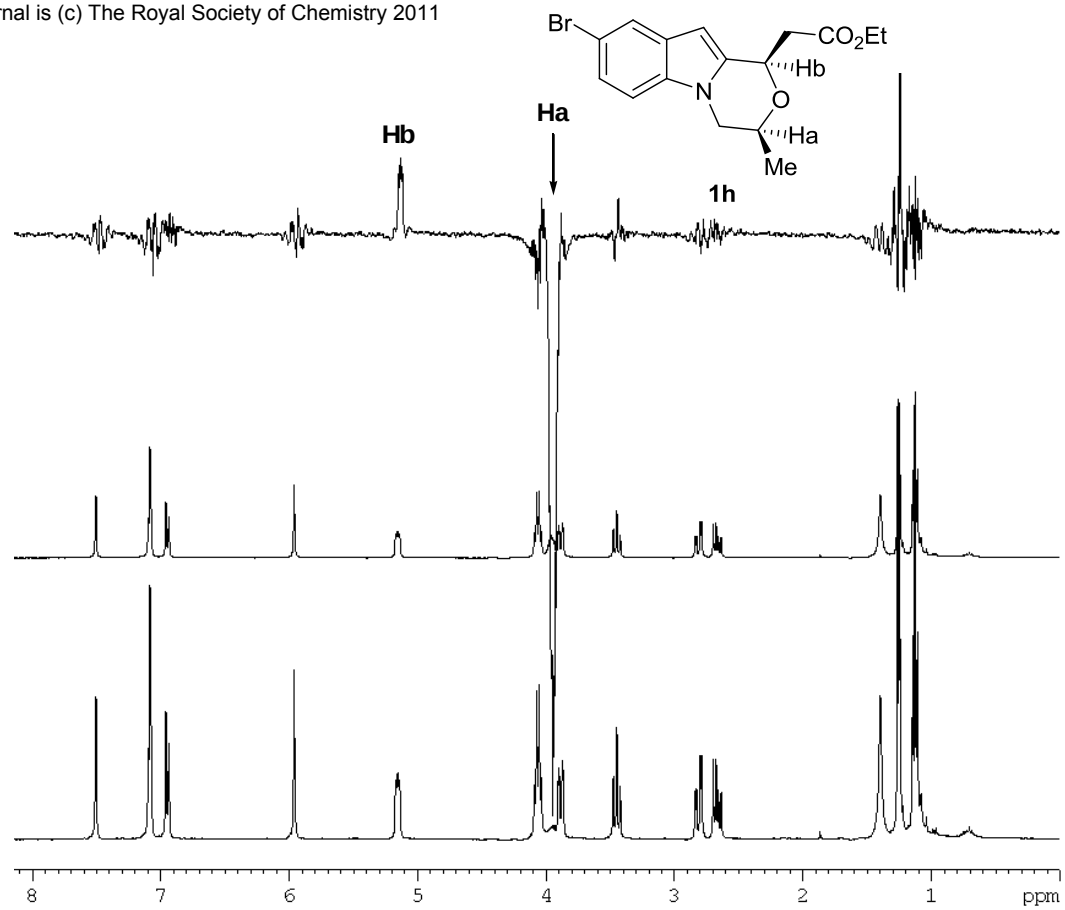
1h

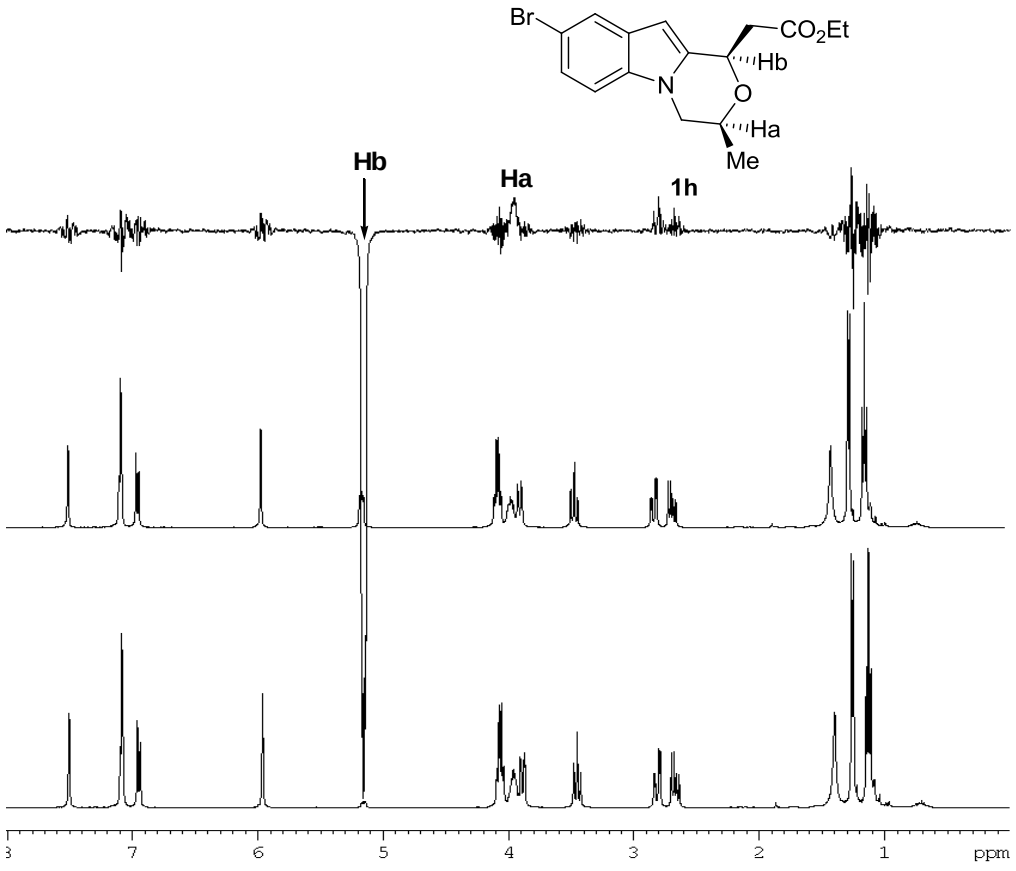
^{1}H NMR in $CDCl_3$

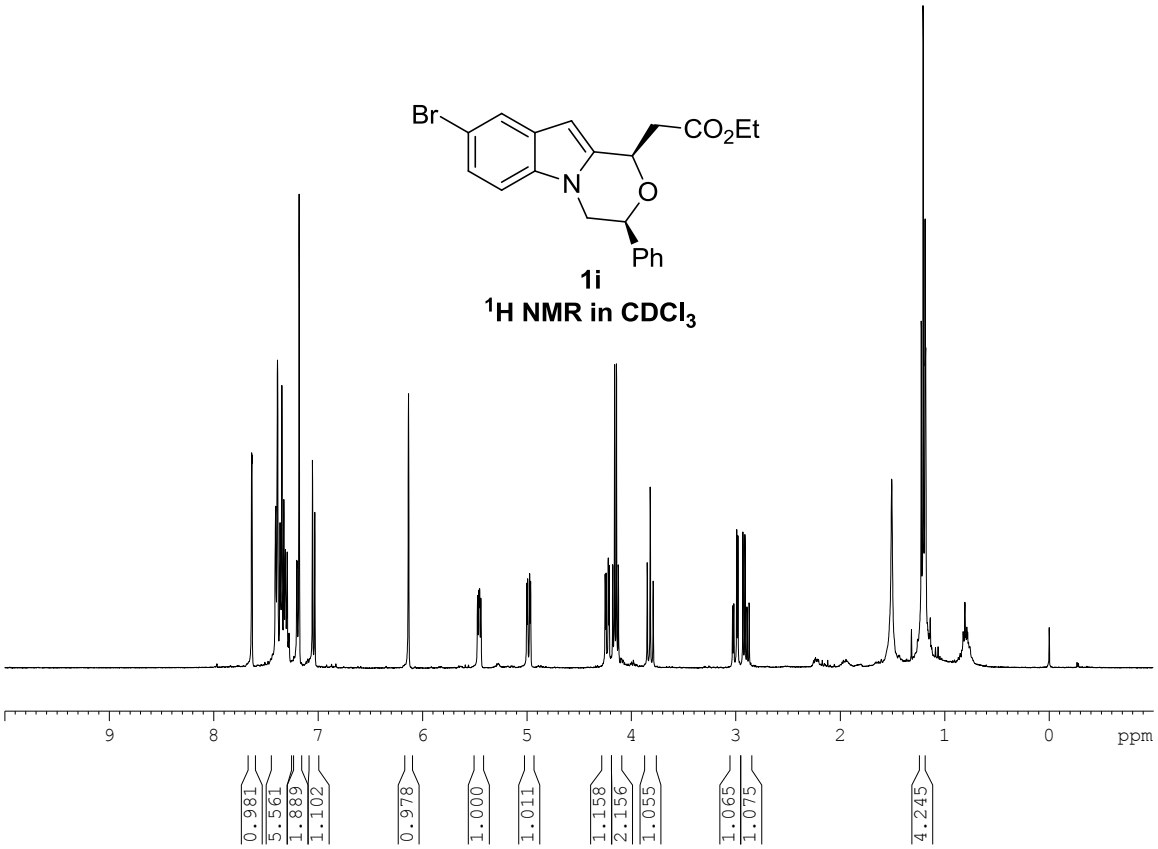


1h

^{13}C NMR in $CDCl_3$

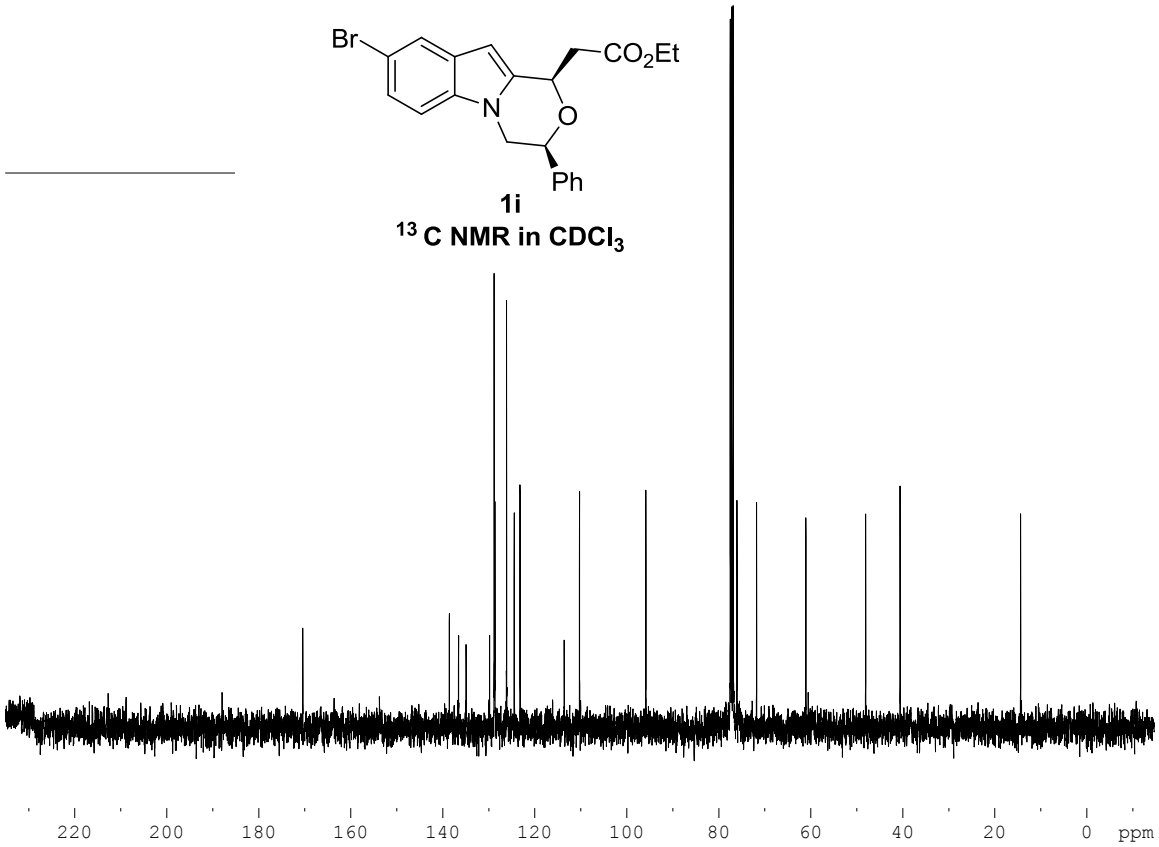

Br
CO2Et
Hb
N
O
Ha
Me
Hb
Ha
1h
8
7
6
5
4
3
2
1
ppm


Br
CO2Et
Hb
N
O
Ha
Me
Hb
Ha
1h
7
6
5
4
3
2
1
ppm



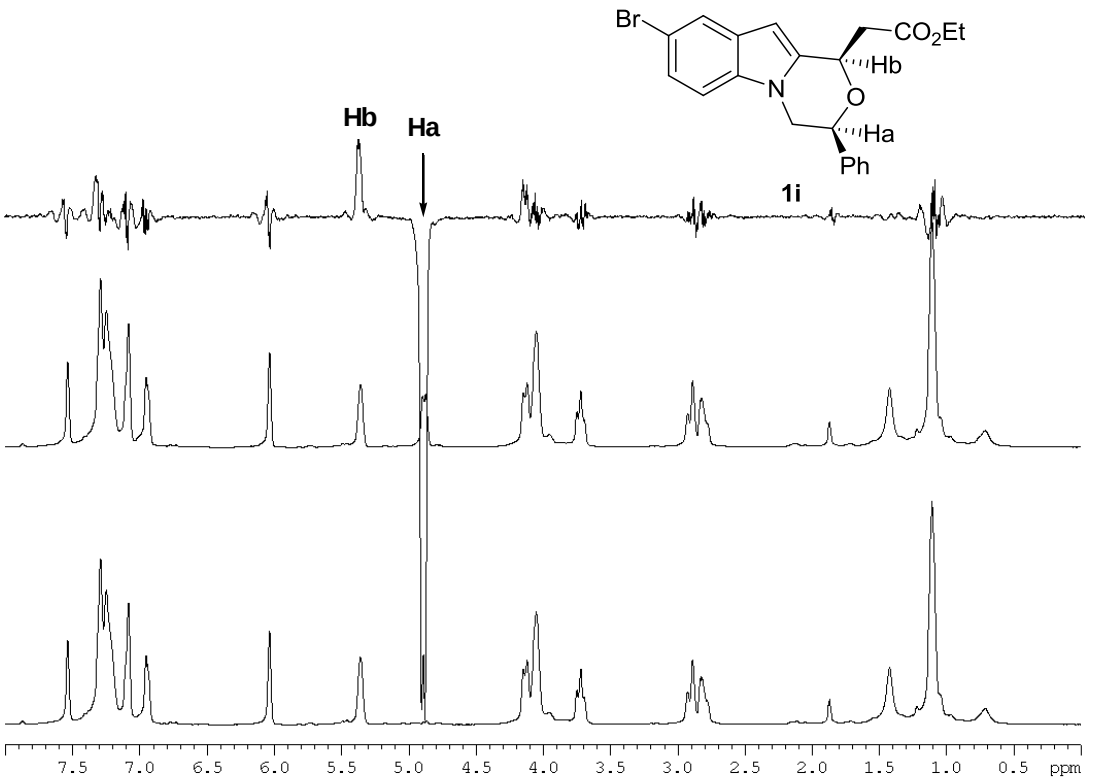
1i

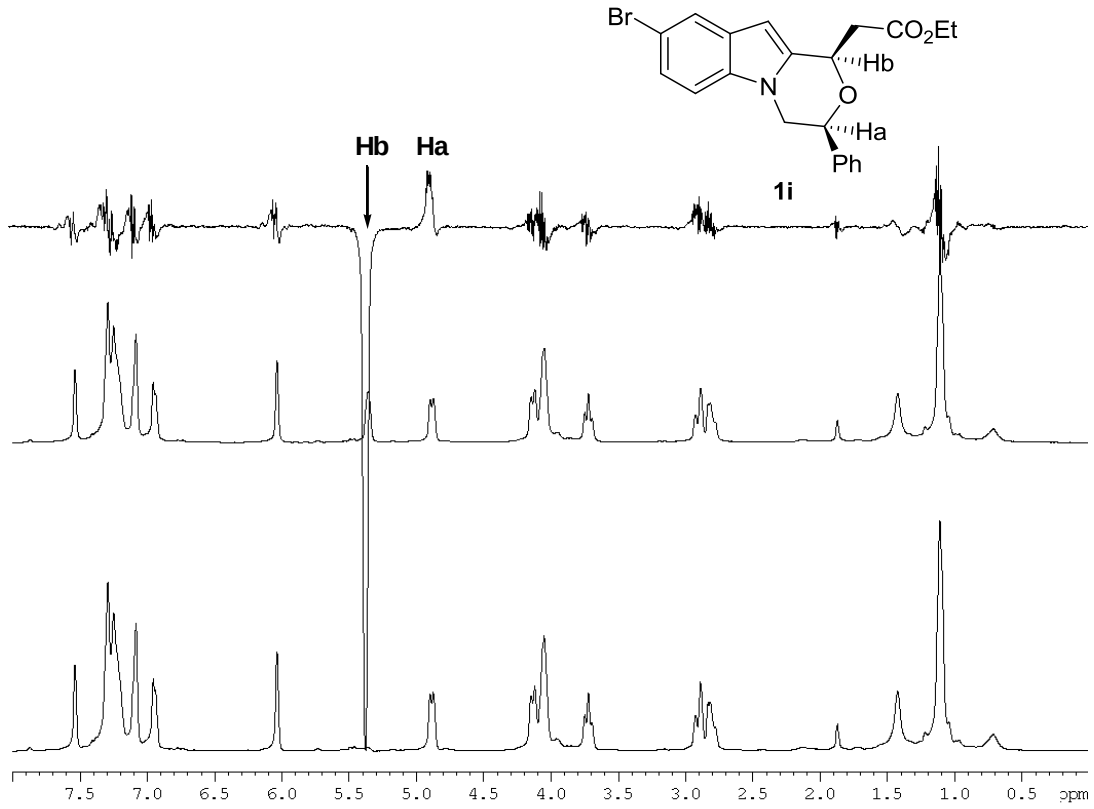
^{1}H NMR in $CDCl_3$

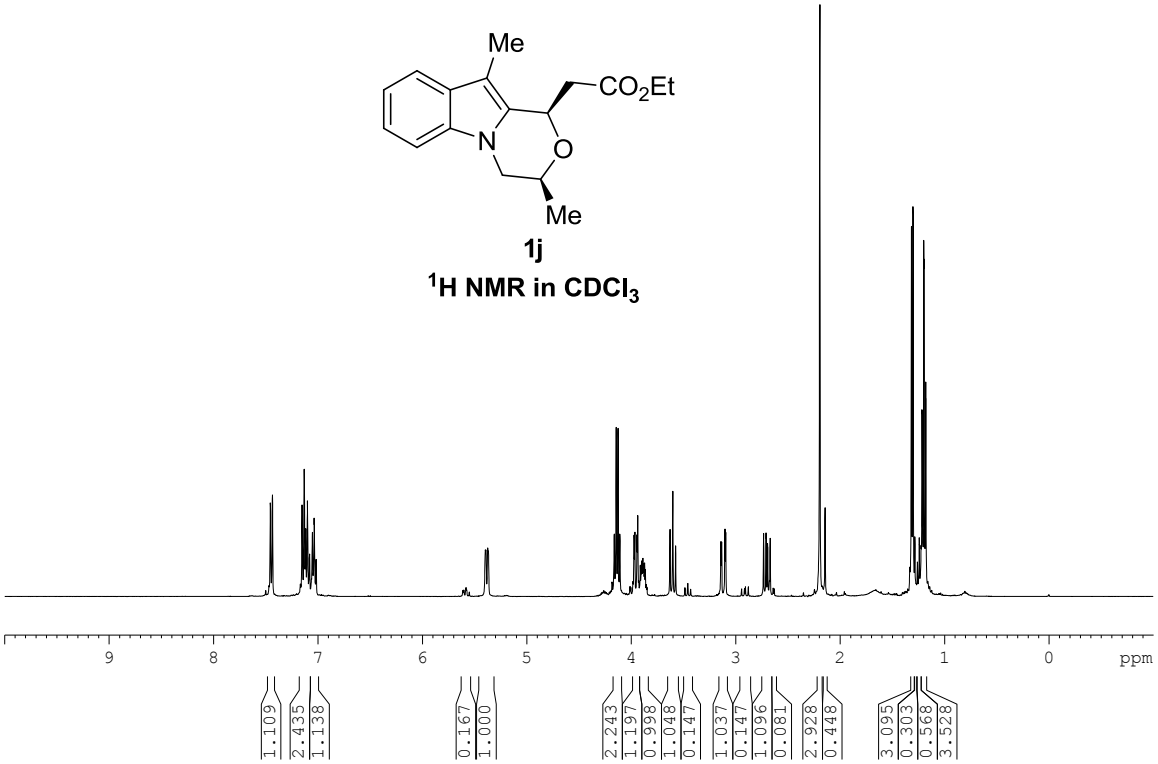


1i

^{13}C NMR in $CDCl_3$

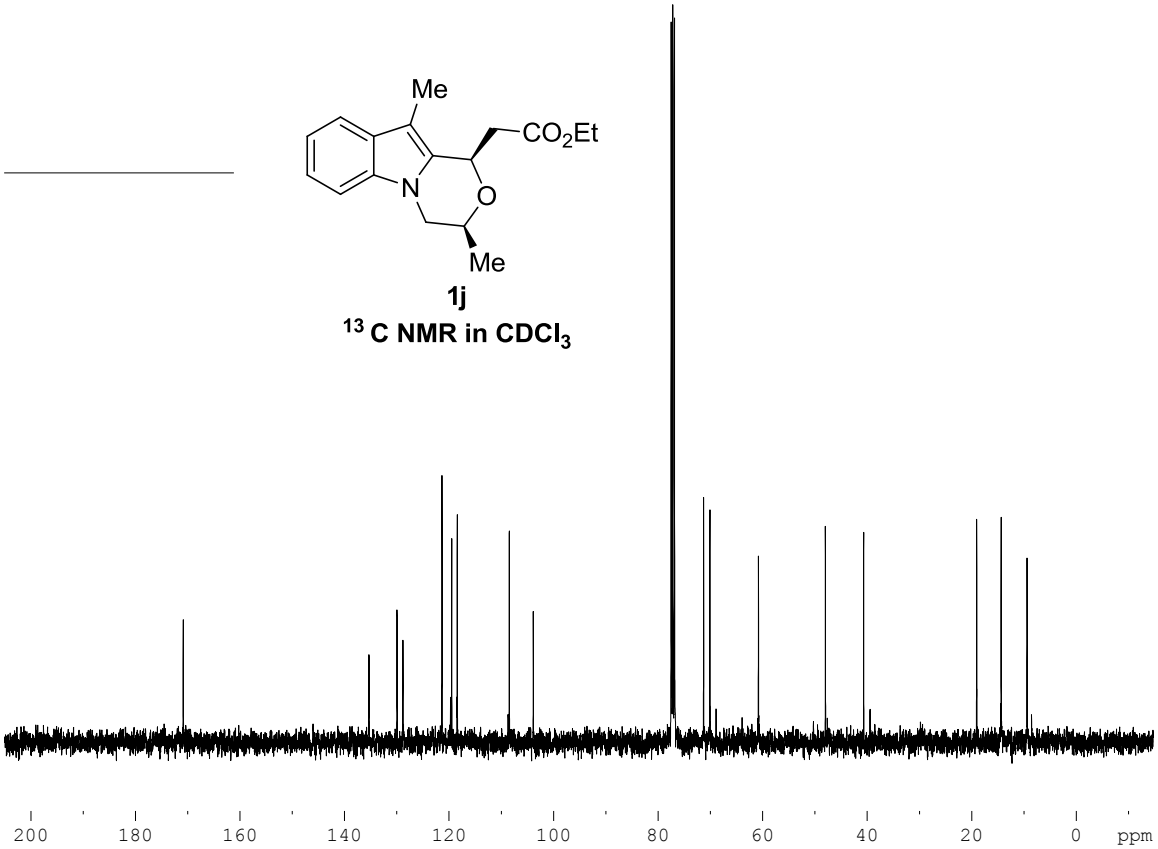

Br
CO2Et
Hb
N
O
Ha
Ph
1i
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Br
CO2Et
Hb
N
O
Ha
Ph
1i
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



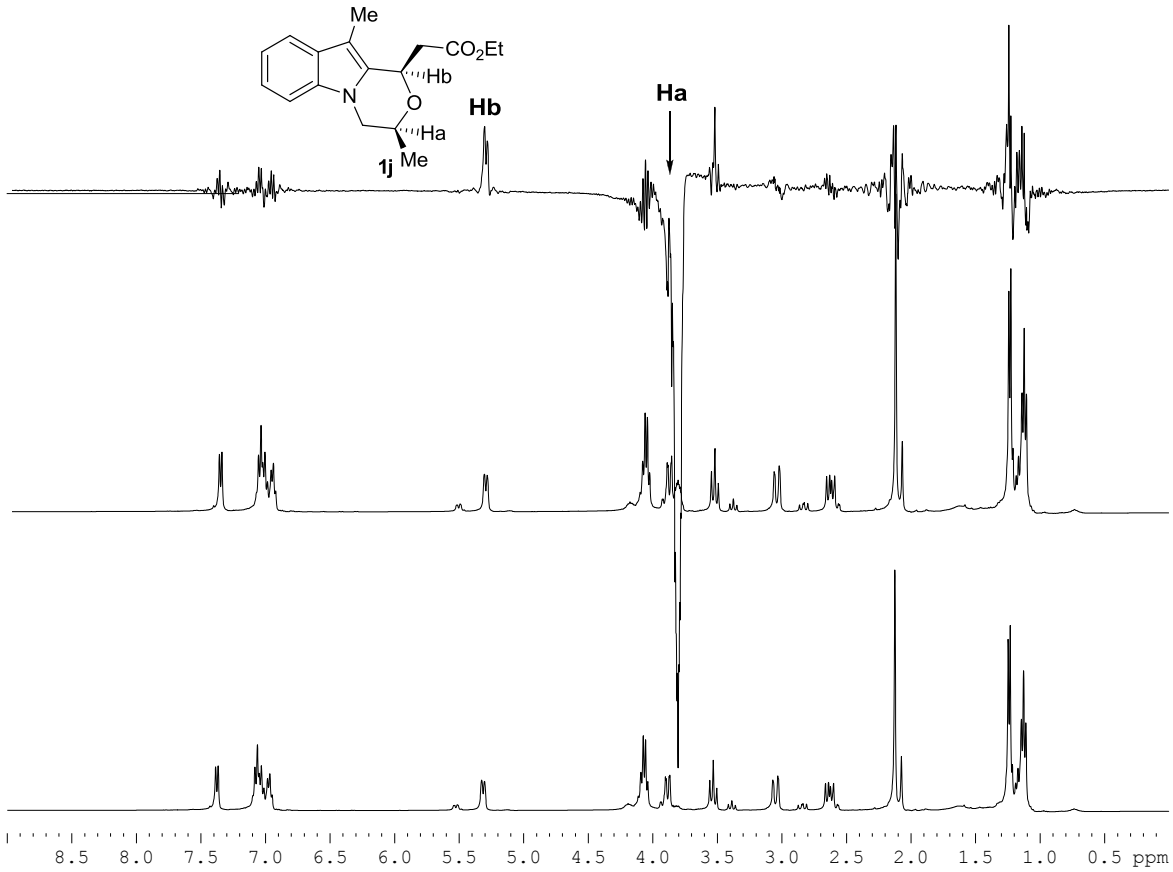
1j

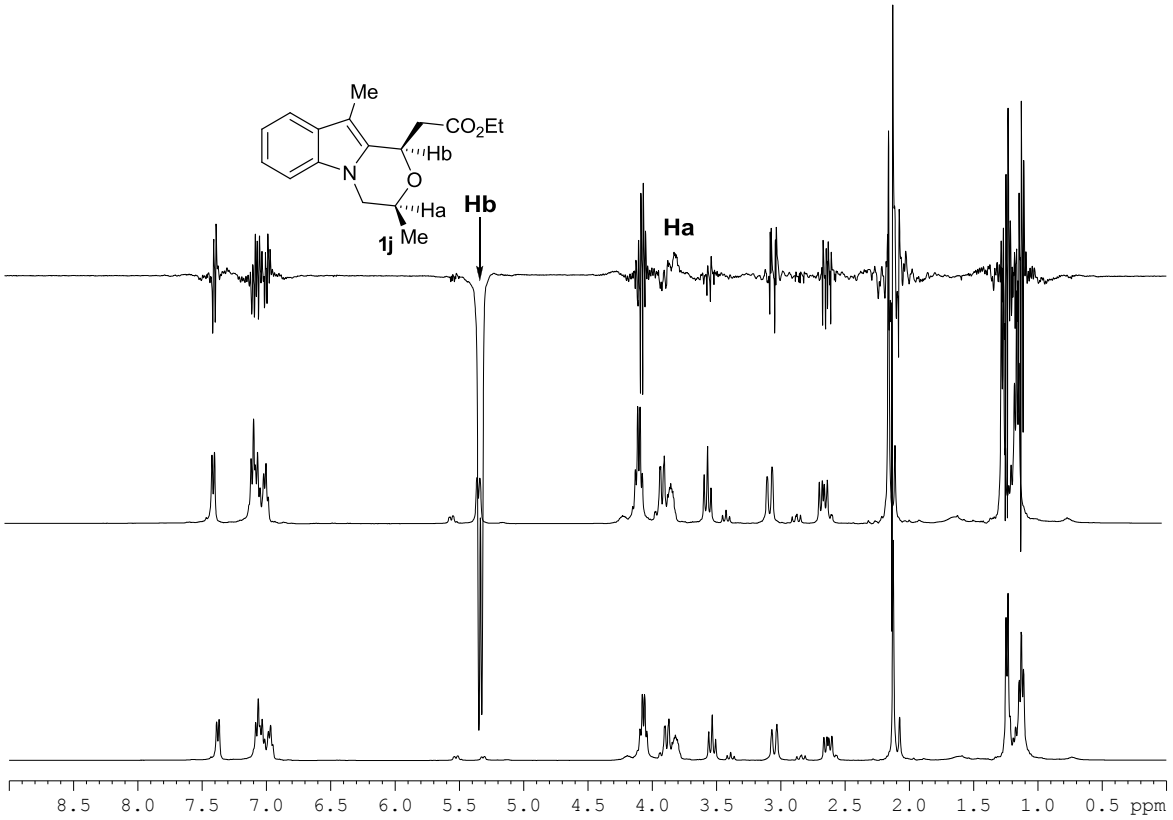
^{1}H NMR in $CDCl_3$

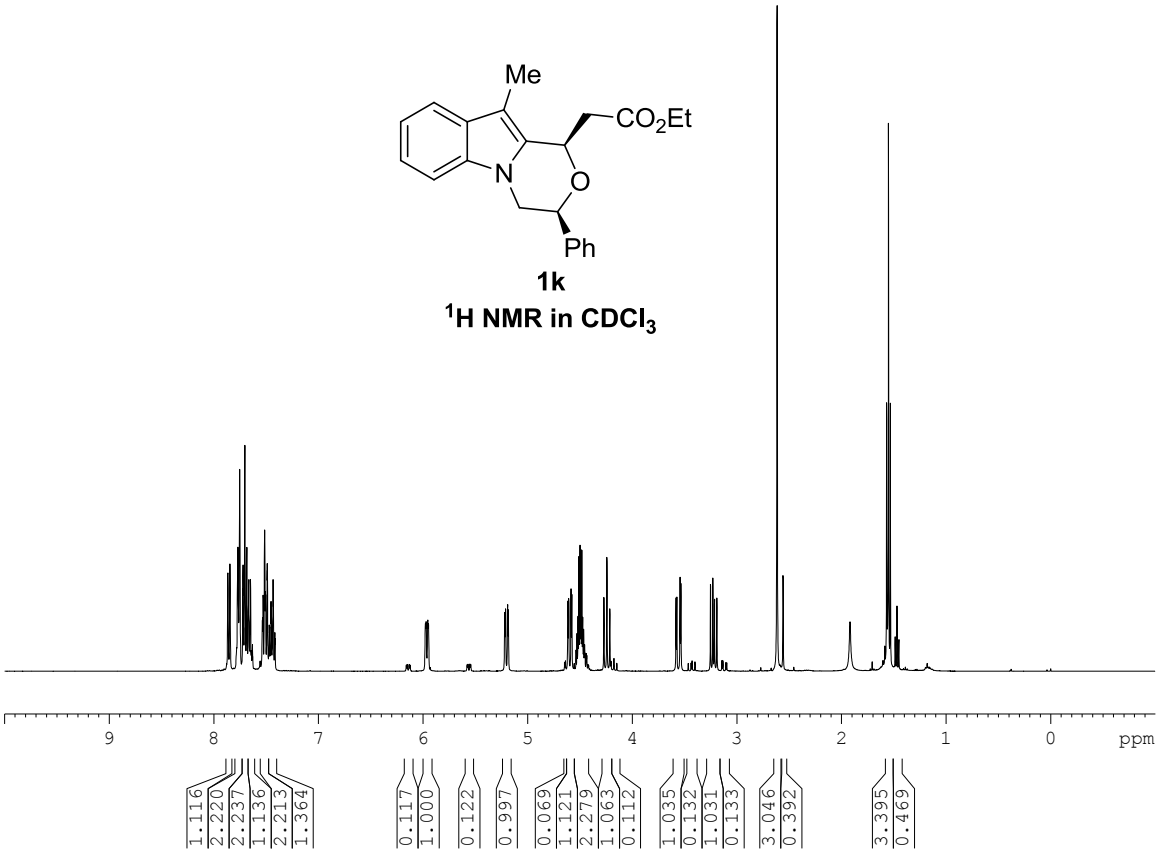


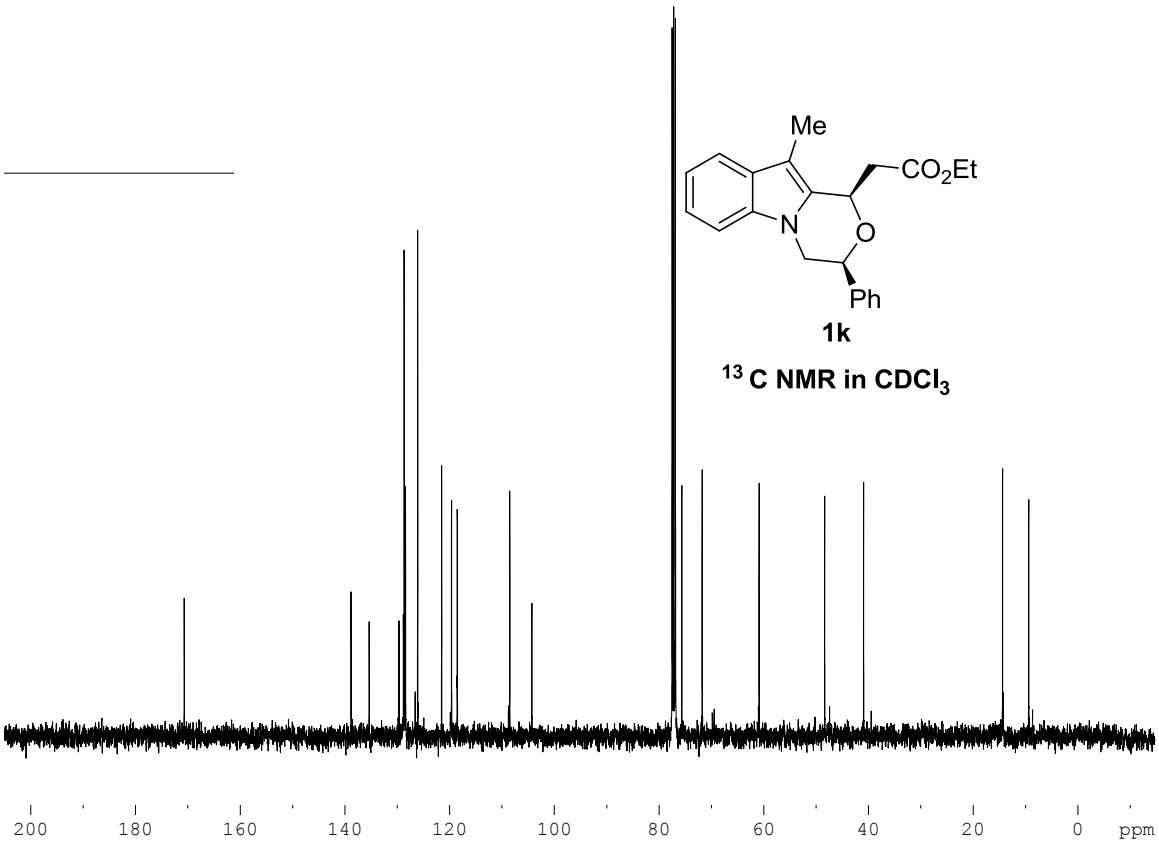
1j

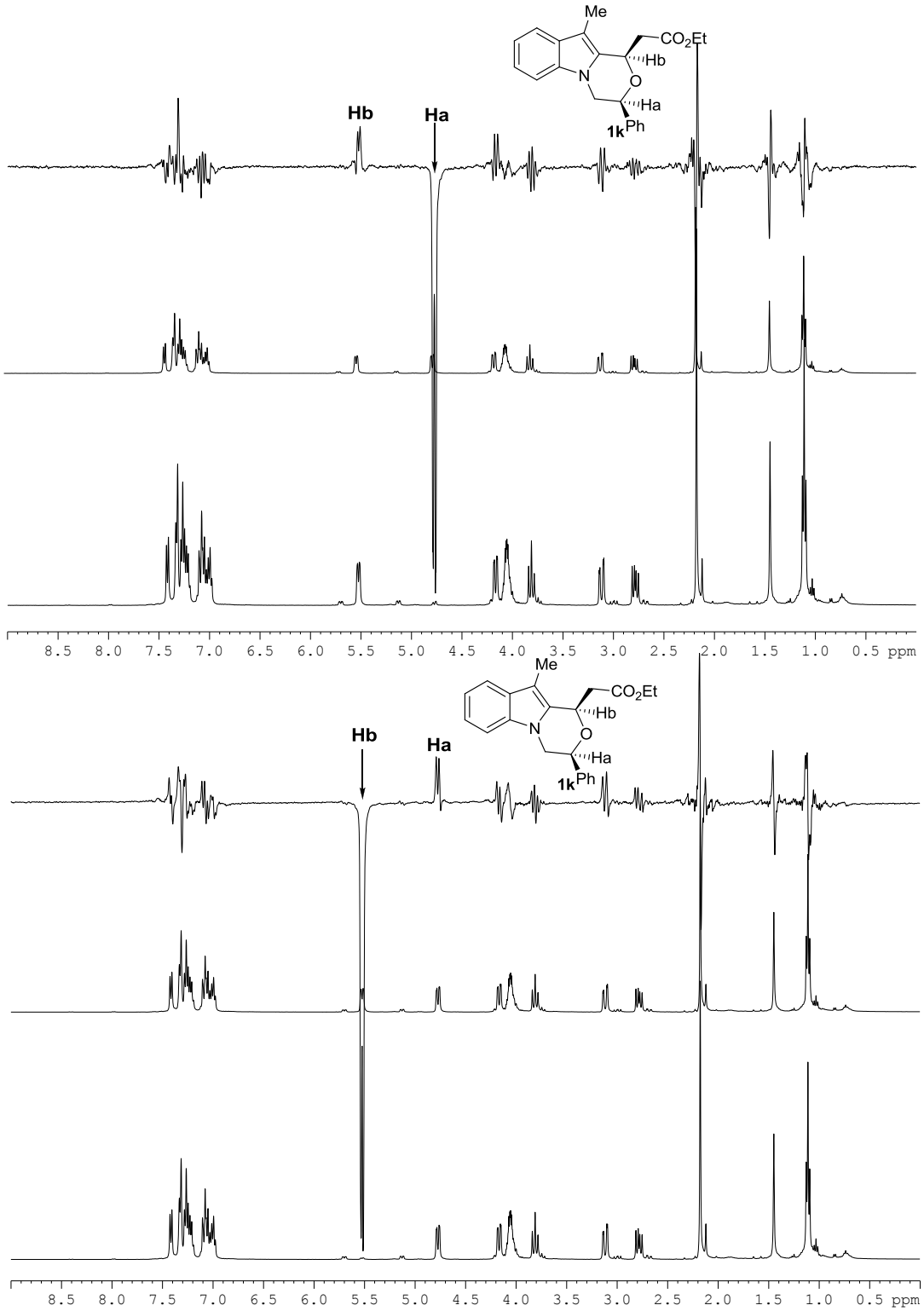
^{13}C NMR in $CDCl_3$

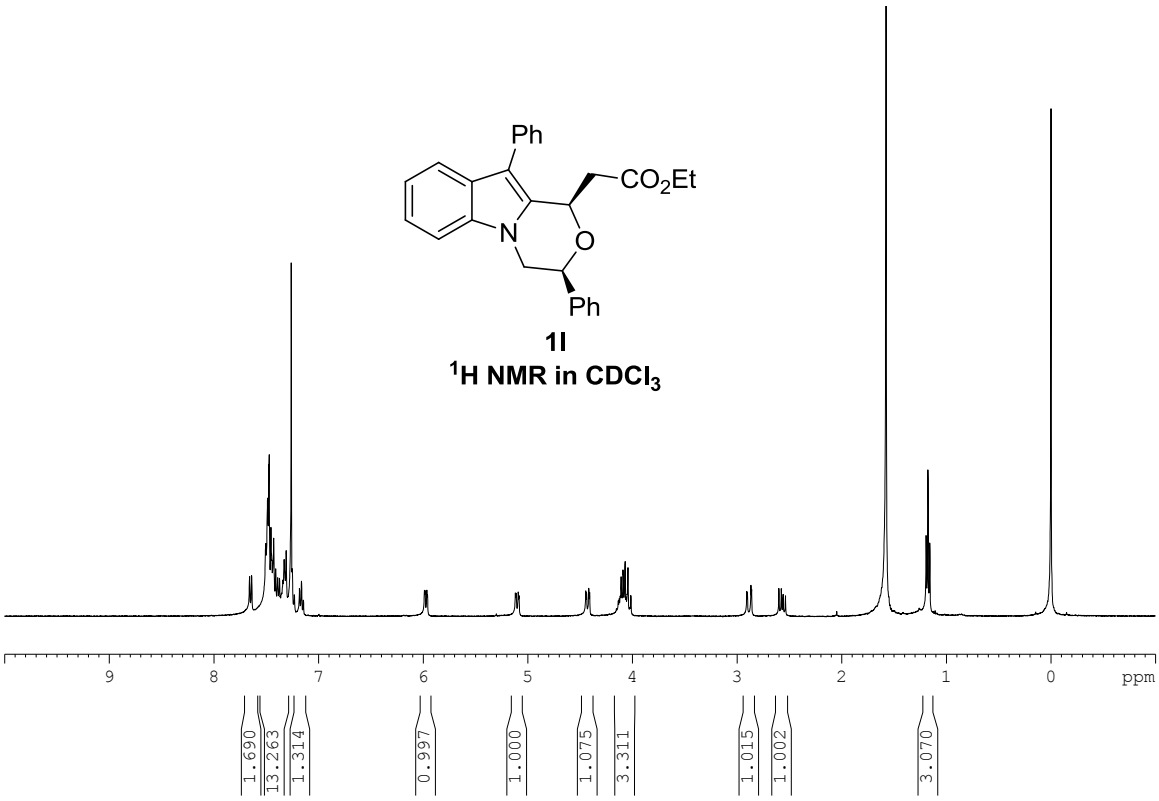

Me
CO2Et
Hb
N
O
Ha
Me
1j
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Me
CO2Et
Hb
N
O
Ha
Me
1j
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Me
CO2Et
N
O
Ph
1k
1H NMR in CDCl3
9
8
7
6
5
4
3
2
1
0
ppm
1.116
2.220
2.237
1.136
2.213
1.364
0.117
1.000
0.122
0.997
0.069
1.121
2.279
1.063
0.112
1.035
0.132
1.031
0.133
3.046
0.392
3.395
0.469

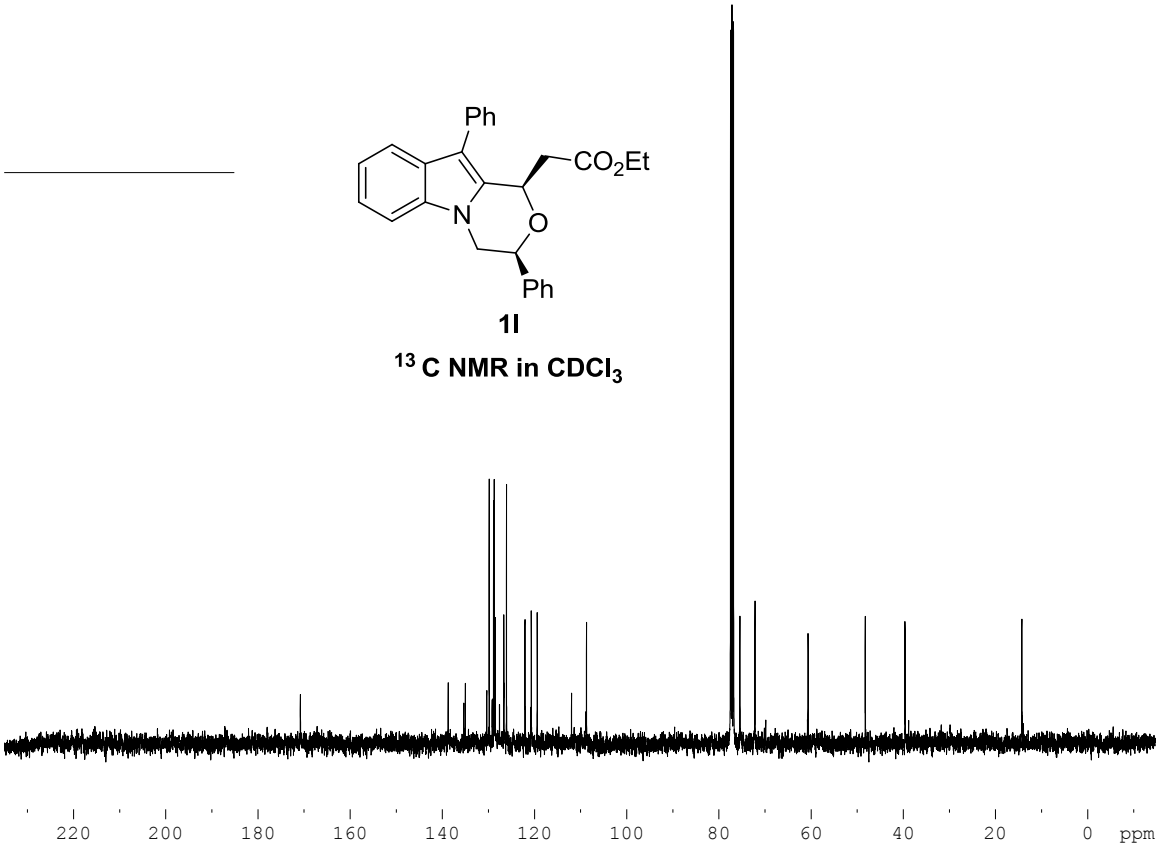

Me
CO2Et
N
O
Ph
1k
13 C NMR in CDCl3
200
180
160
140
120
100
80
60
40
20
0
ppm


Me
CO2Et
Hb
N
O
Ha
1k Ph
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
Me
CO2Et
Hb
N
O
Ha
1k Ph
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



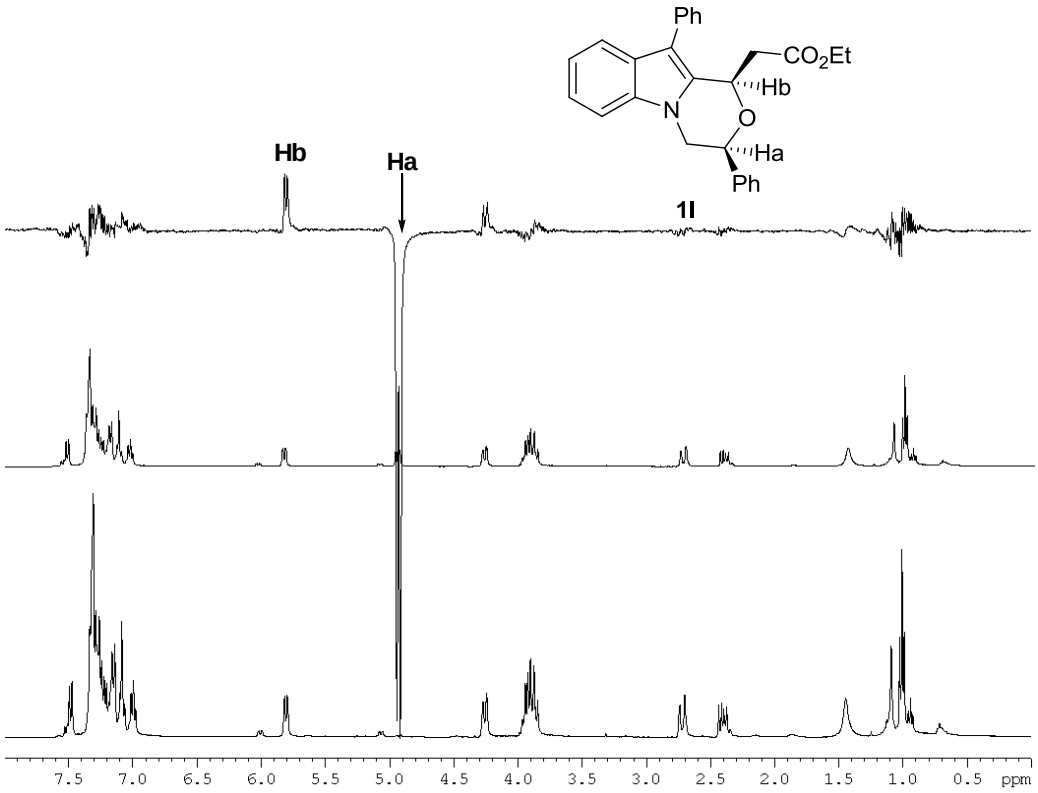
1l

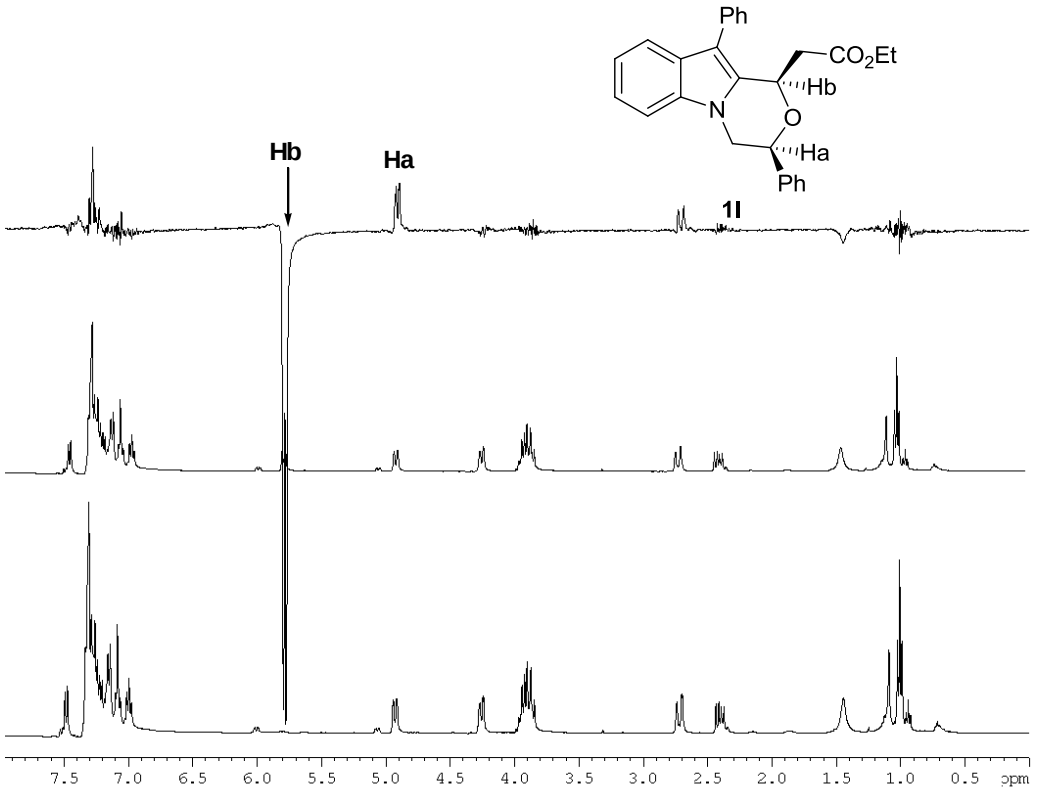
^{1}H NMR in $CDCl_3$

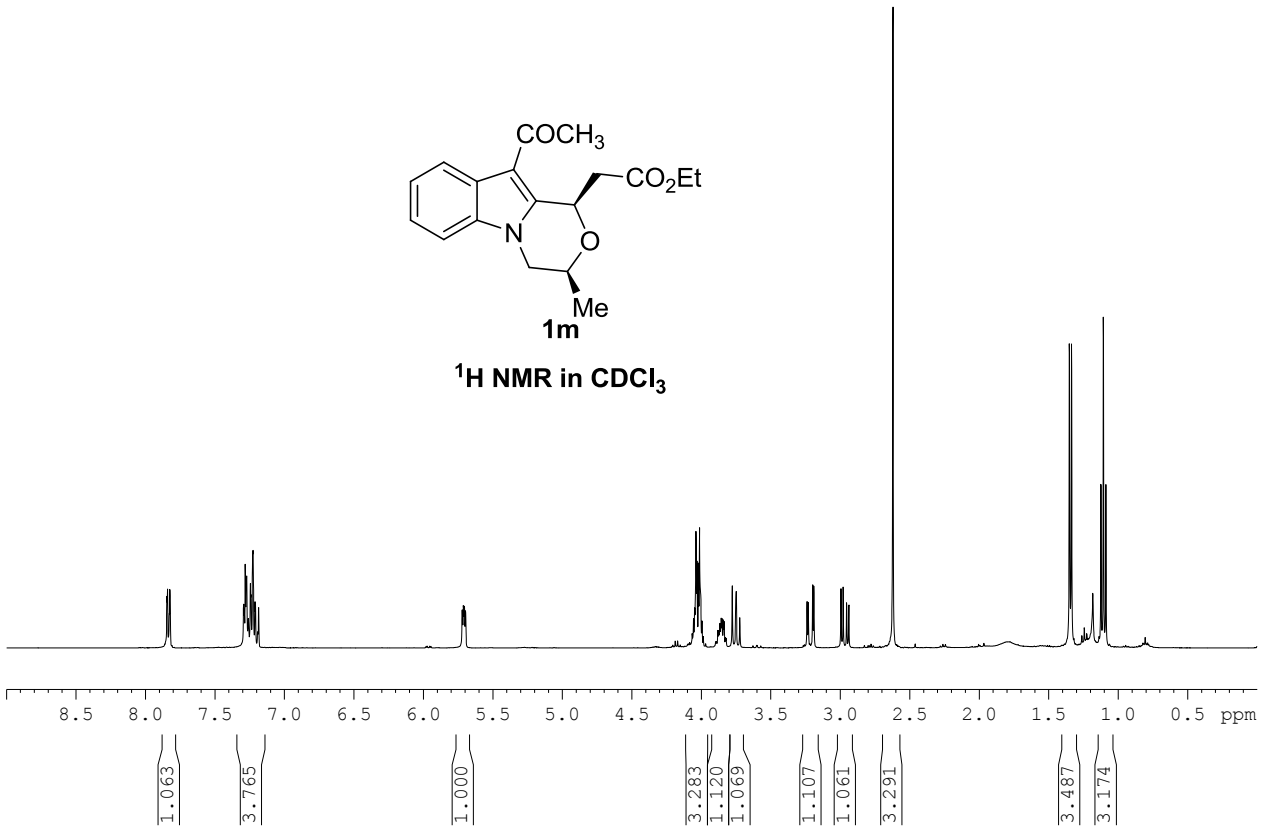


1l

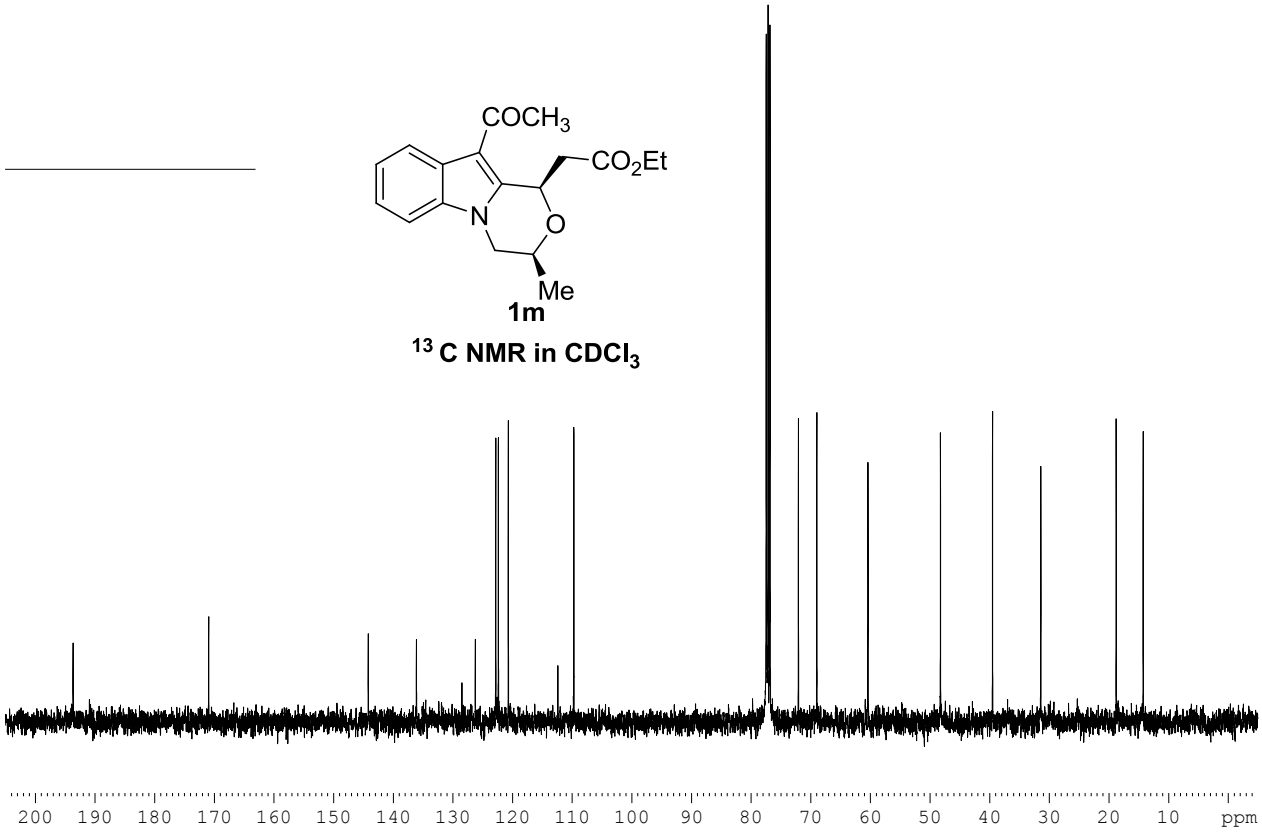
^{13}C NMR in $CDCl_3$


Ph
CO2Et
Hb
N
O
Ha
Ph
Hb
Ha
1l
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

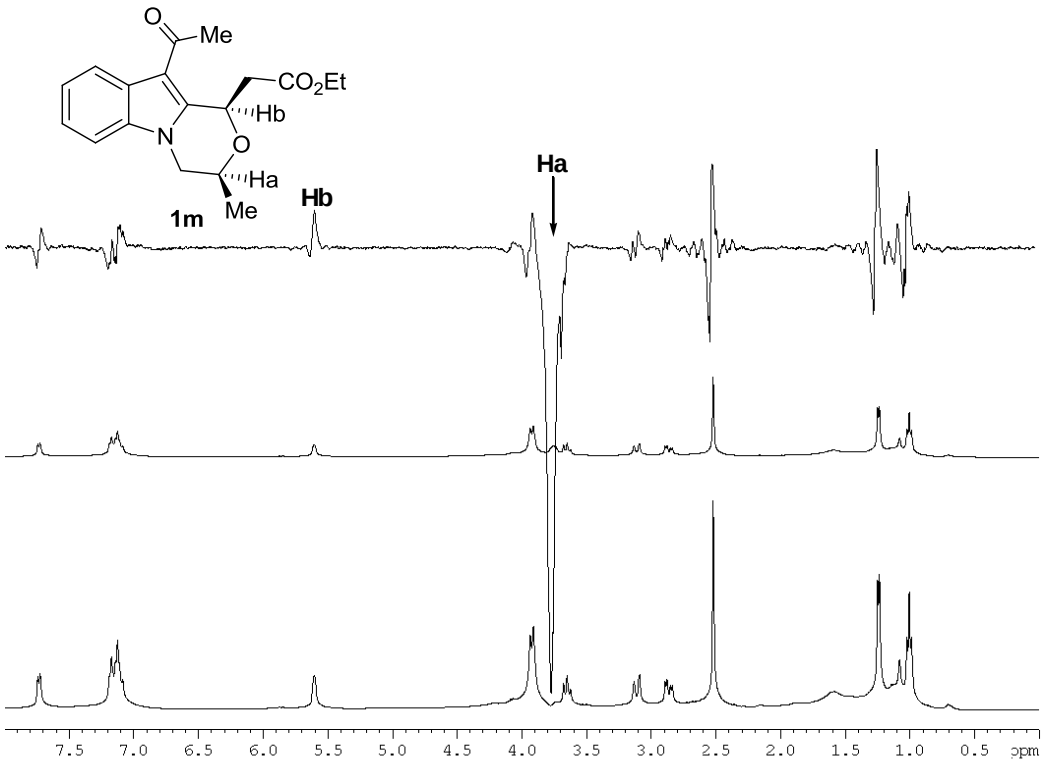

Ph
CO2Et
Hb
N
O
Ha
Ph
Hb
Ha
1l
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

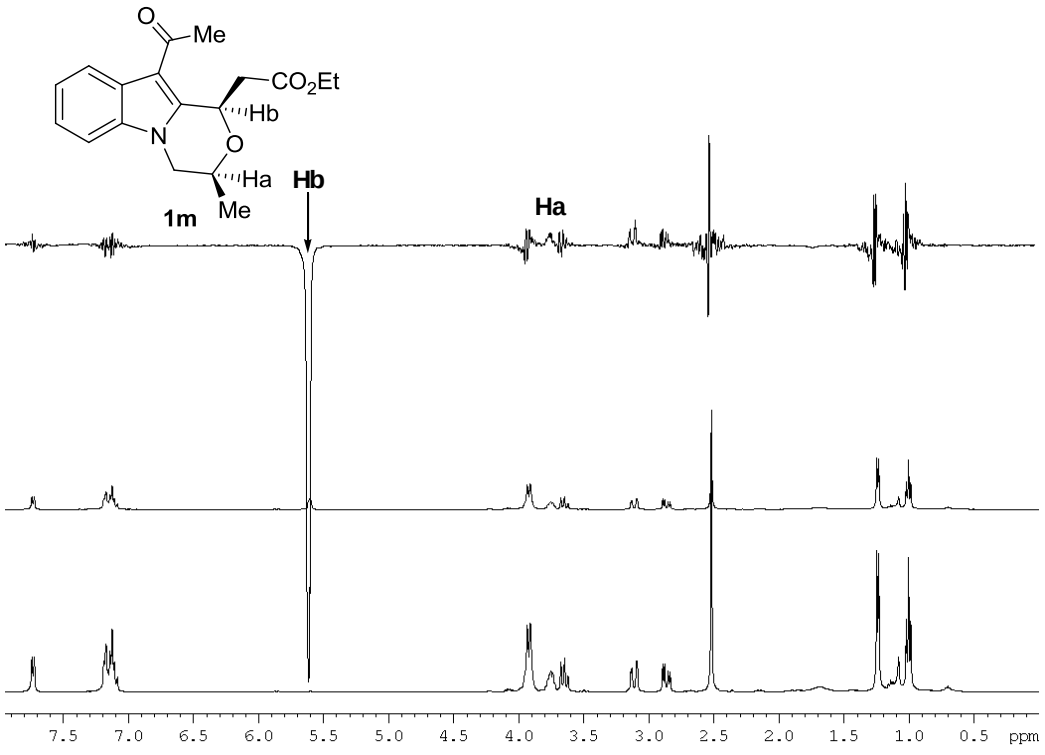


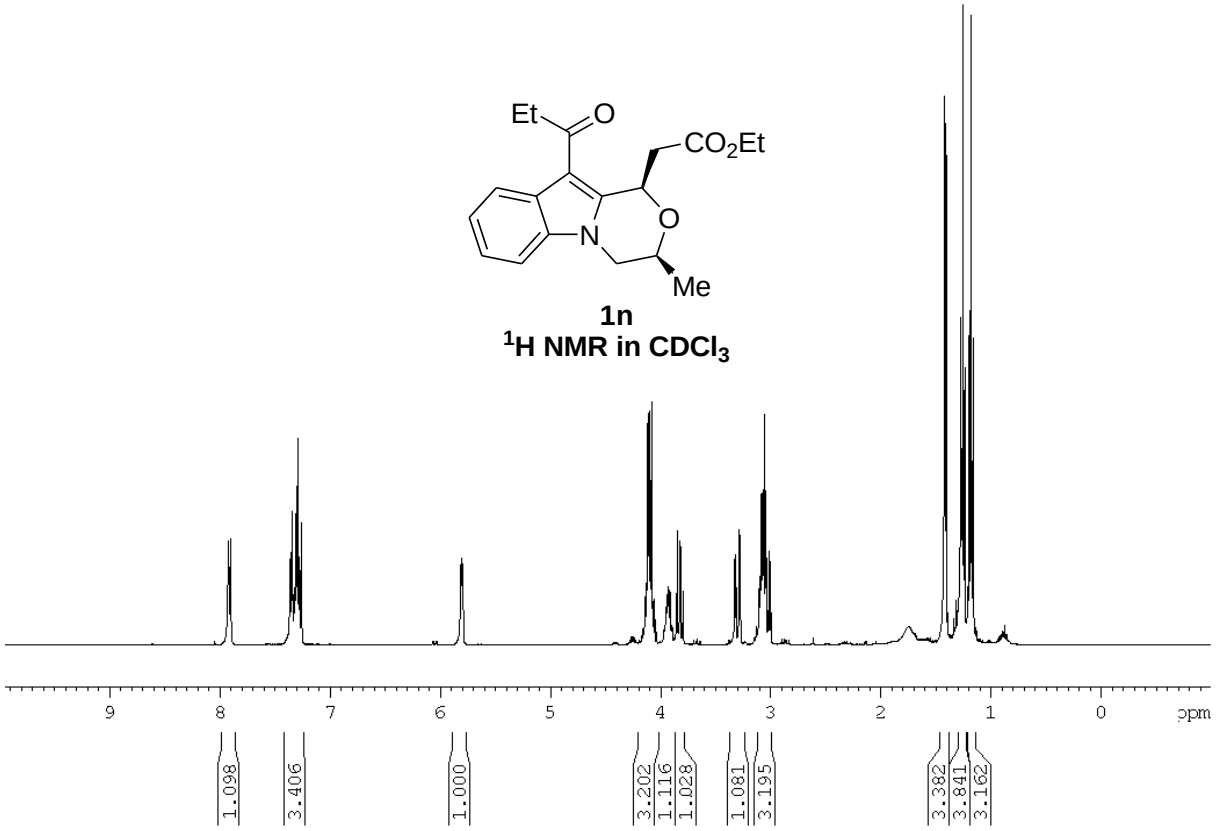
^{1}H NMR in $CDCl_3$



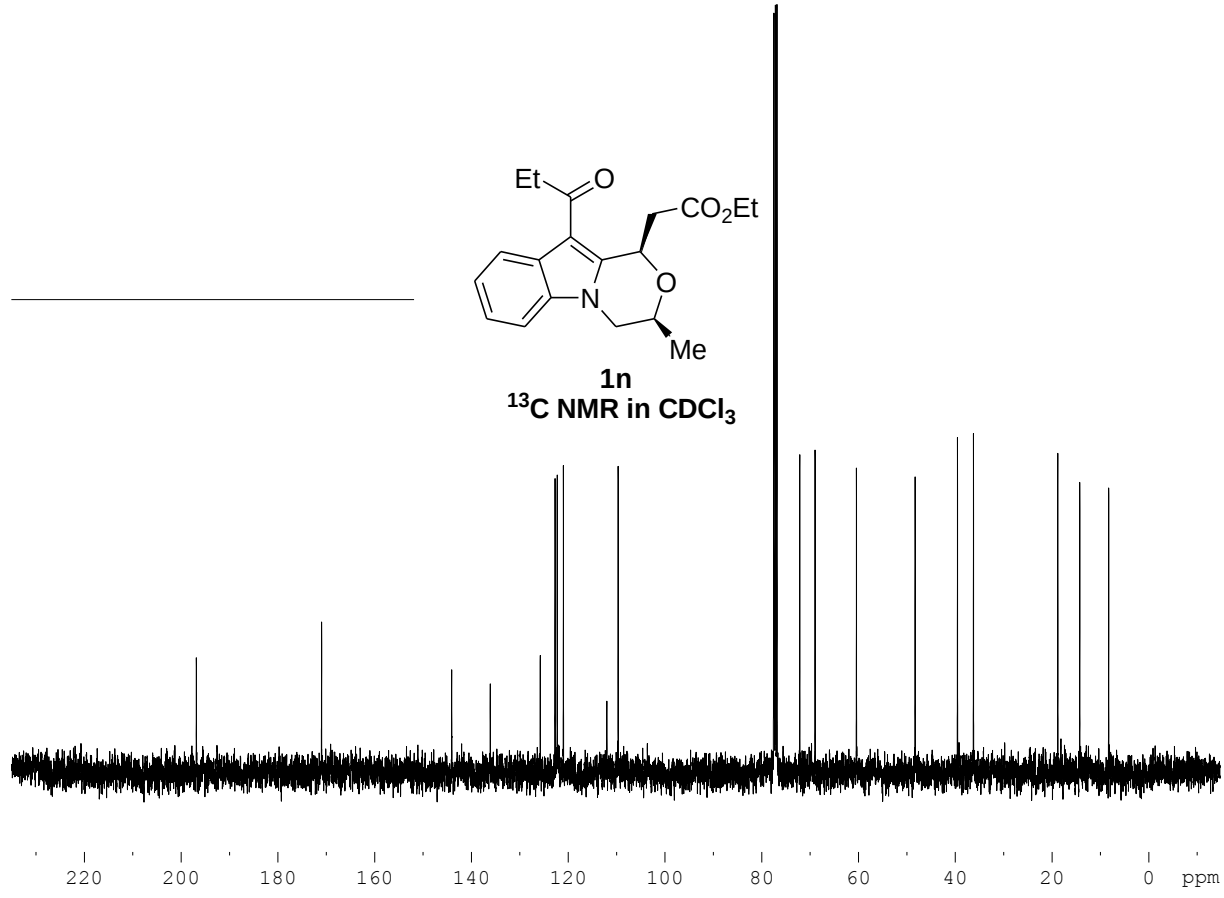
^{13}C NMR in $CDCl_3$


O
Me
CO2Et
Hb
N
O
Ha
Me
1m
Ha
Hb
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

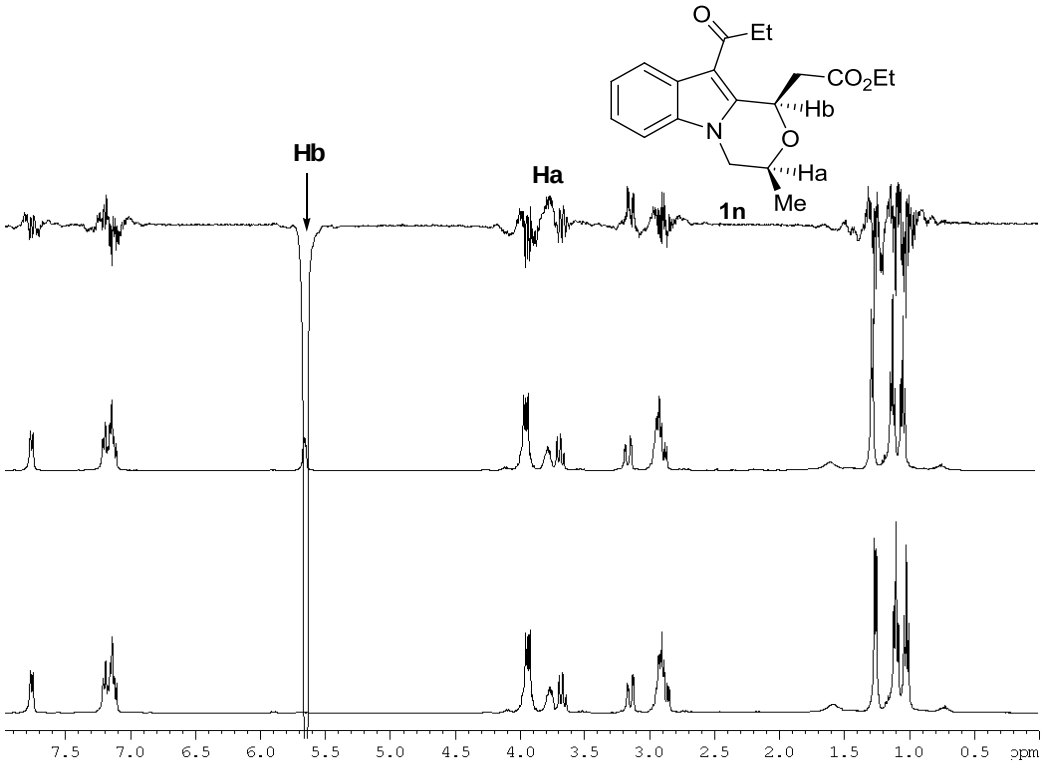

O
Me
CO2Et
Hb
N
O
Ha
Me
1m
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

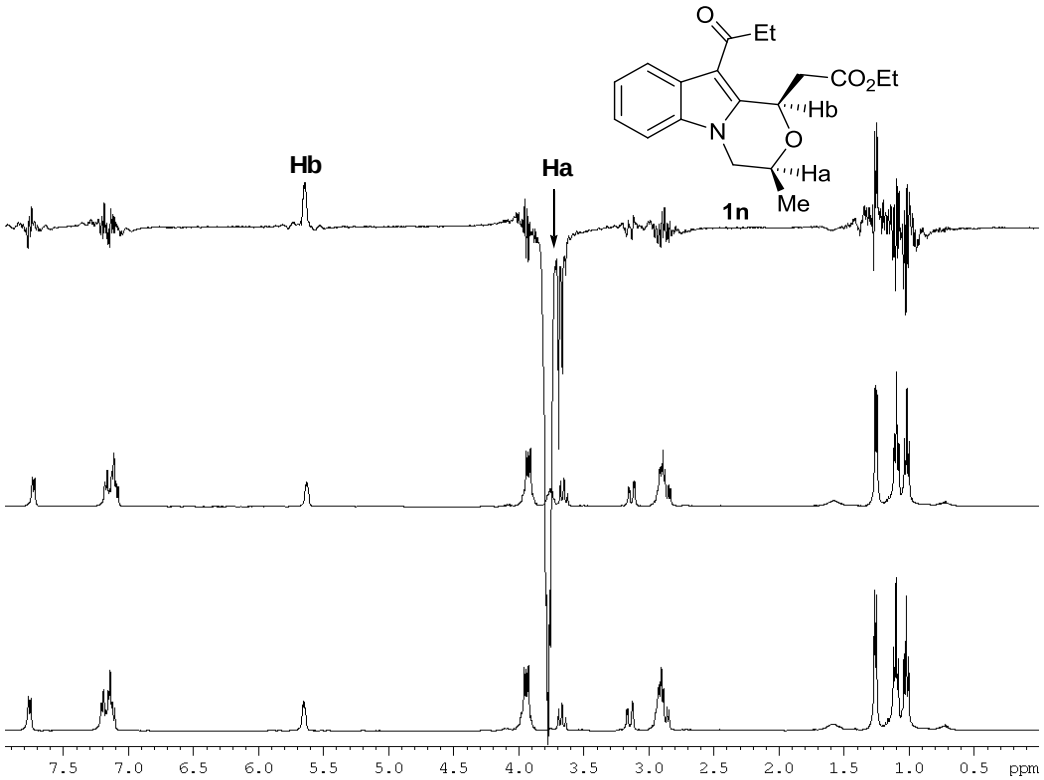


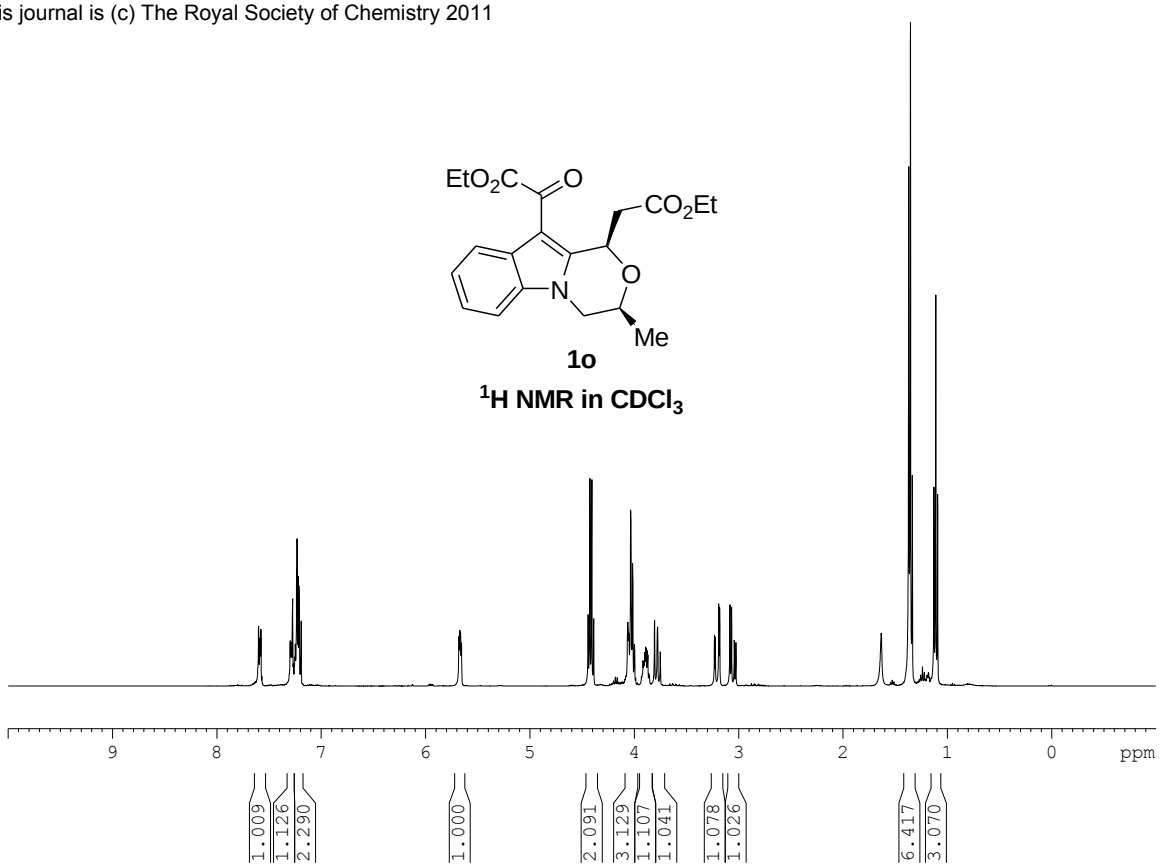
1n
^{1}H NMR in $CDCl_3$



1n
^{13}C NMR in $CDCl_3$

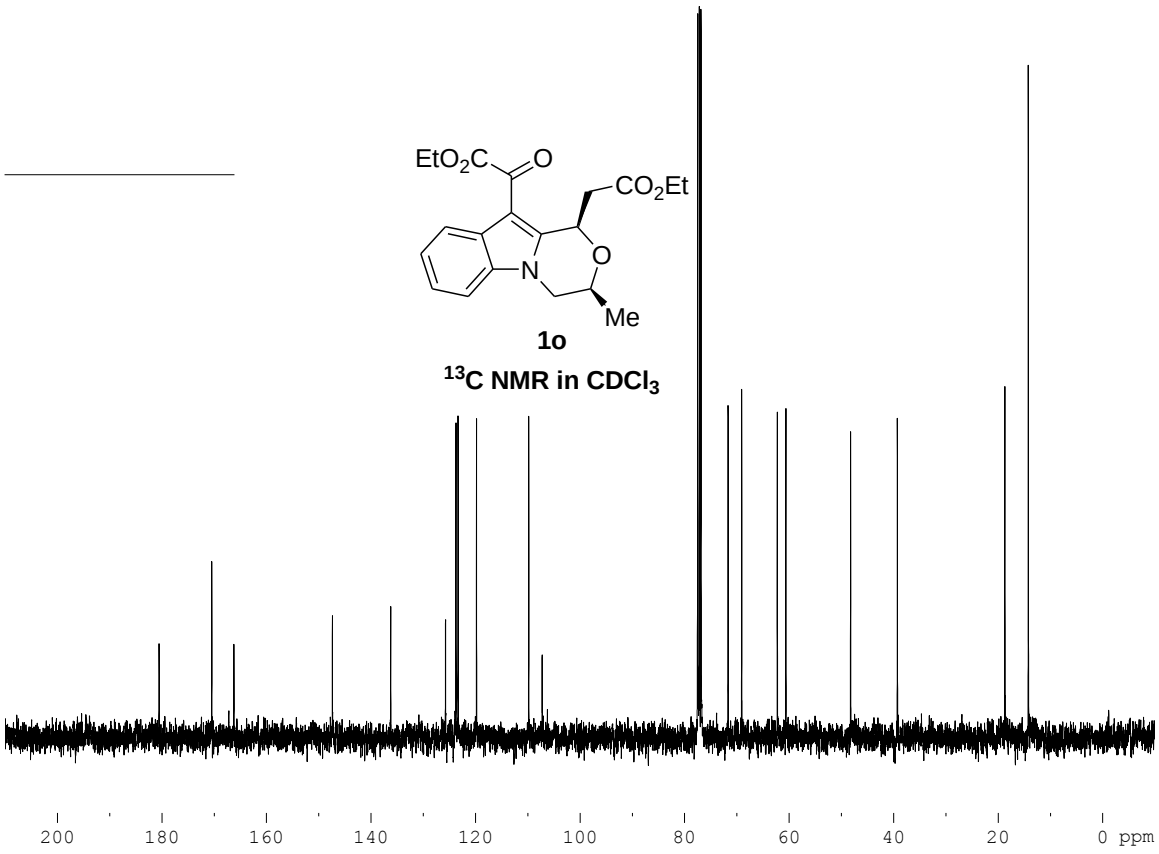

O
Et
CO2Et
Hb
N
O
Ha
Me
1n
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


O
Et
CO2Et
Hb
N
O
Ha
Me
1n
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



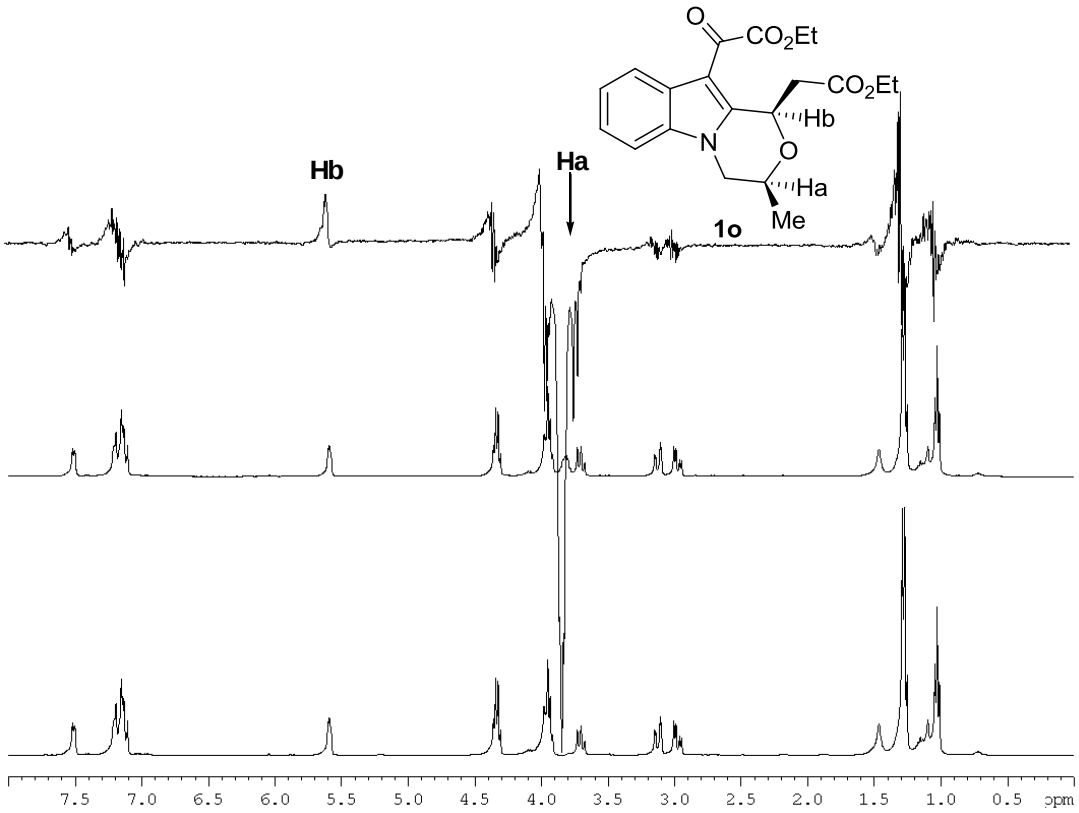
1o

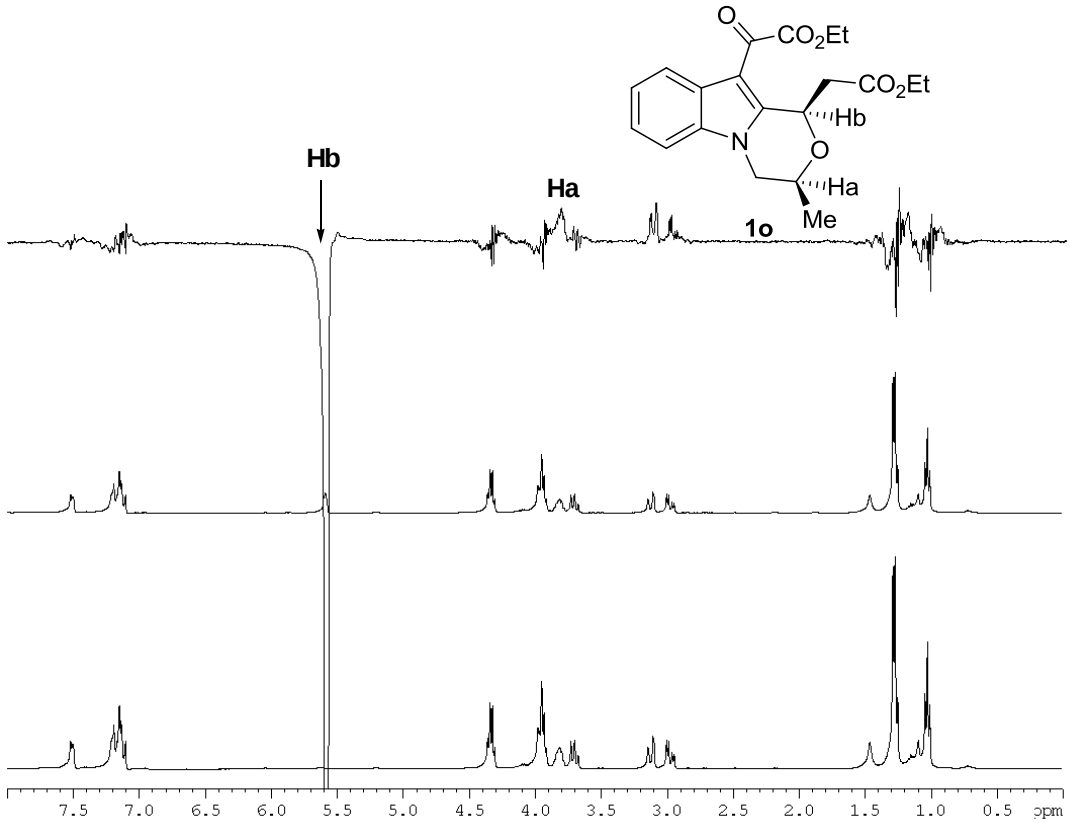
^{1}H NMR in $CDCl_3$

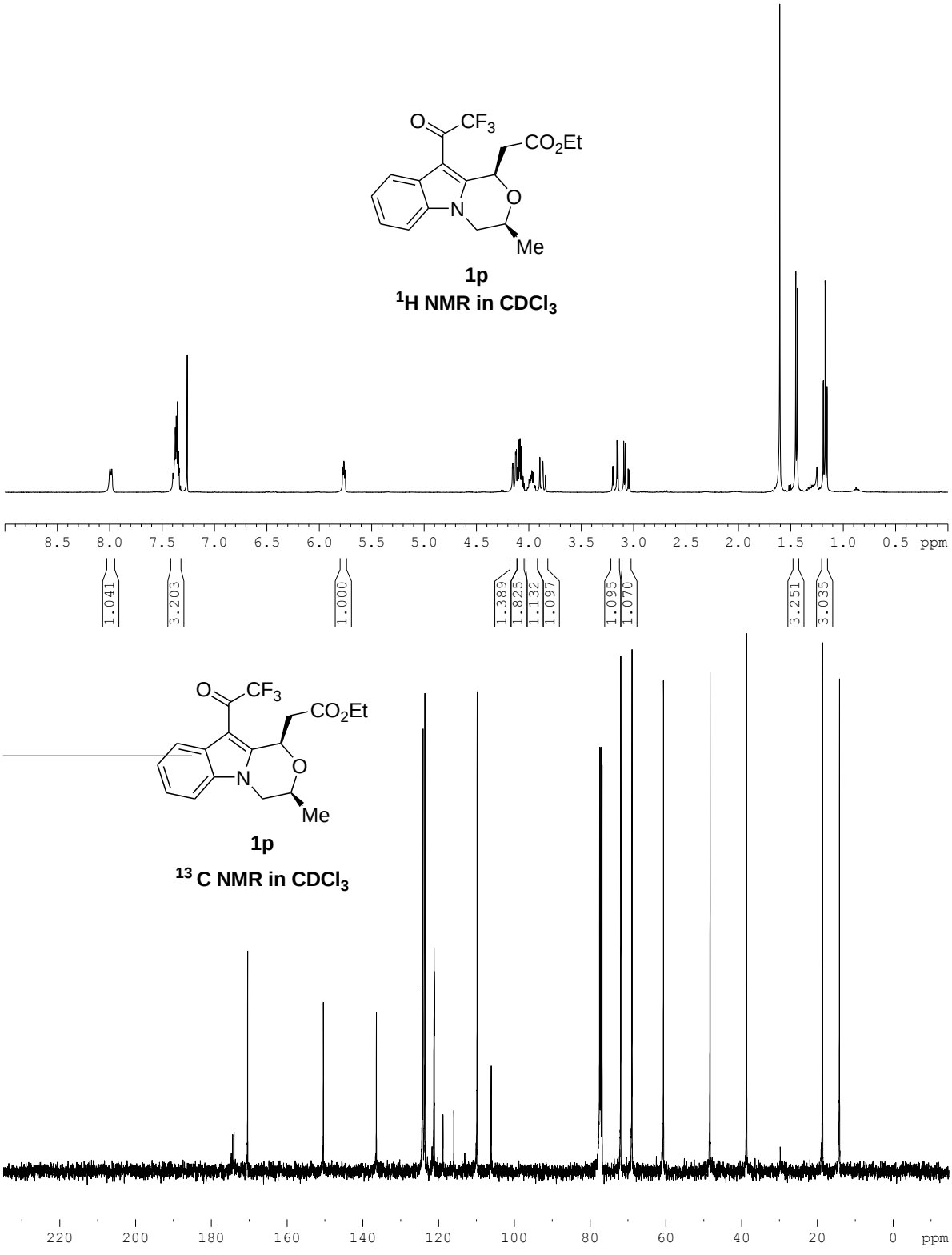


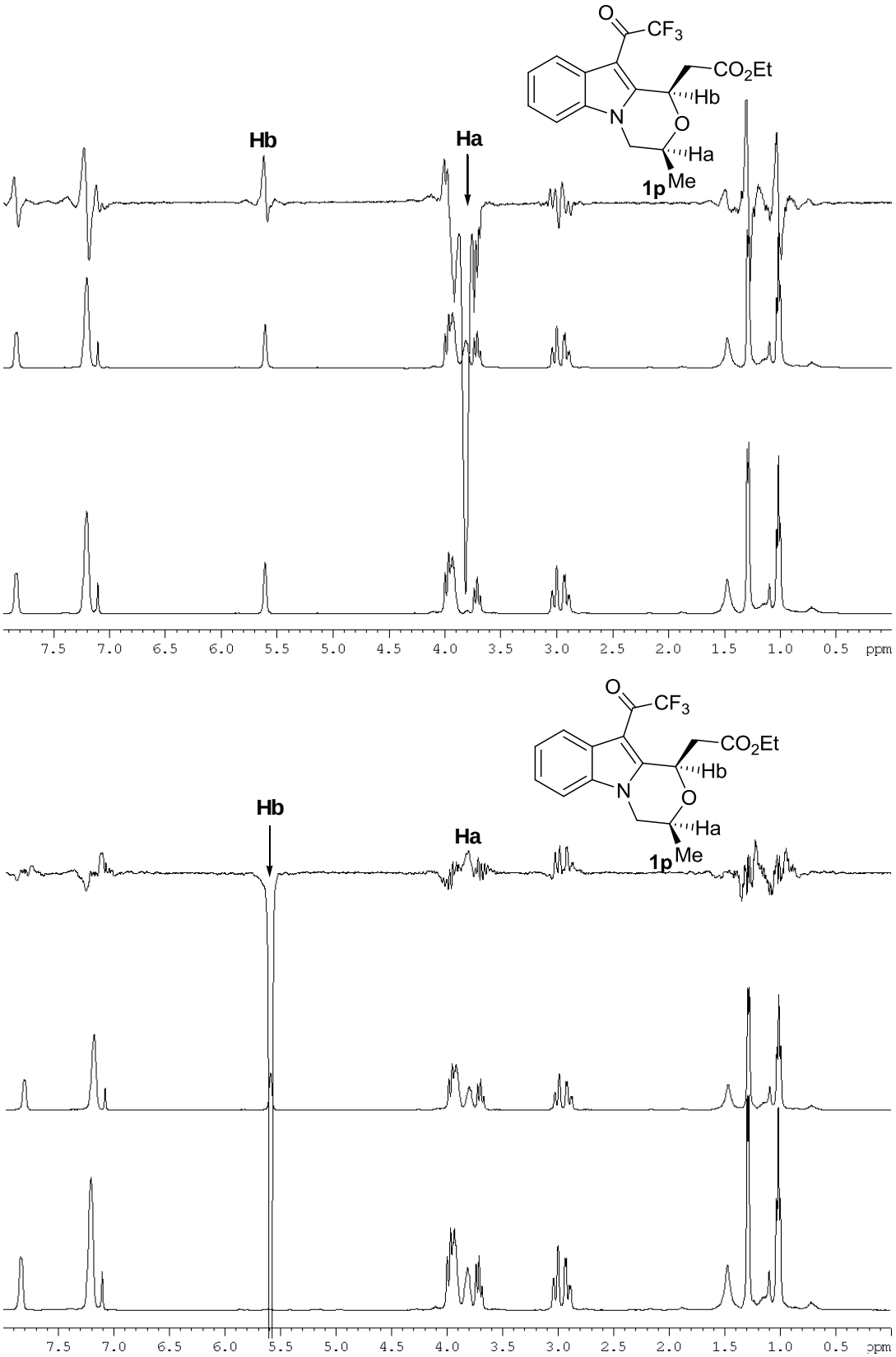
1o

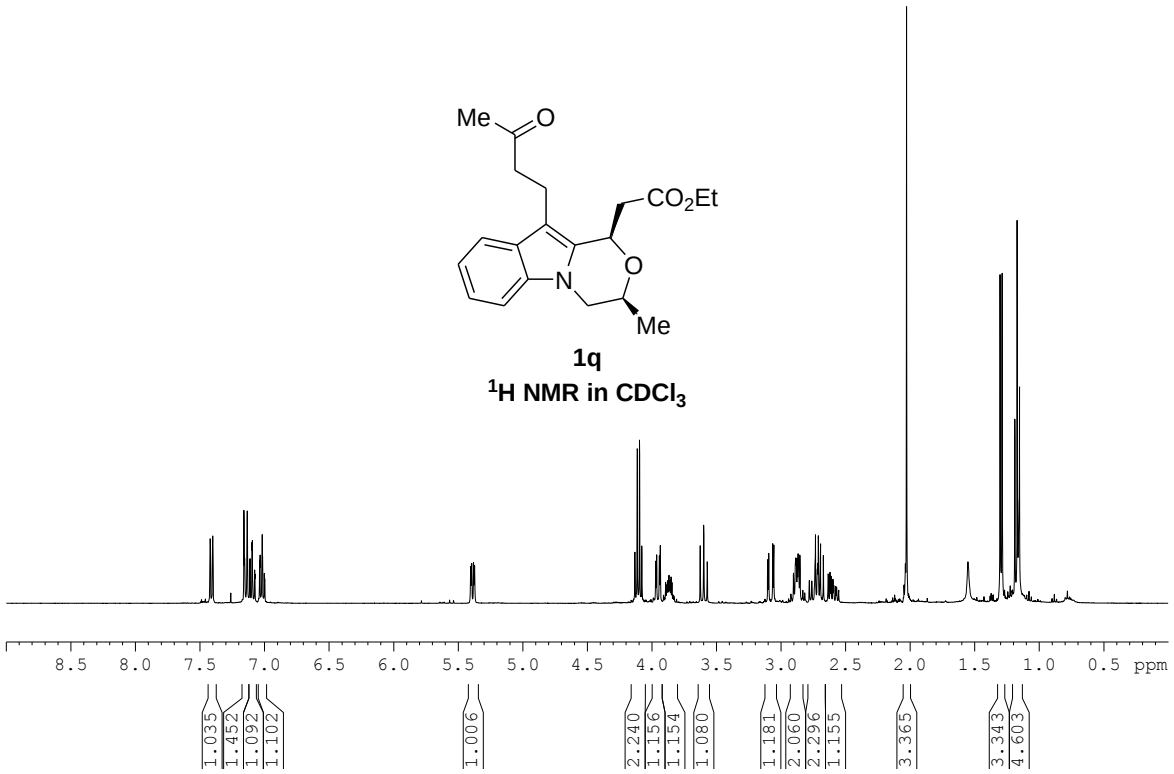
^{13}C NMR in $CDCl_3$


O
CO2Et
CO2Et
Hb
N
O
Ha
Me
1o
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


O
CO2Et
CO2Et
Hb
N
O
Ha
Me
1o
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

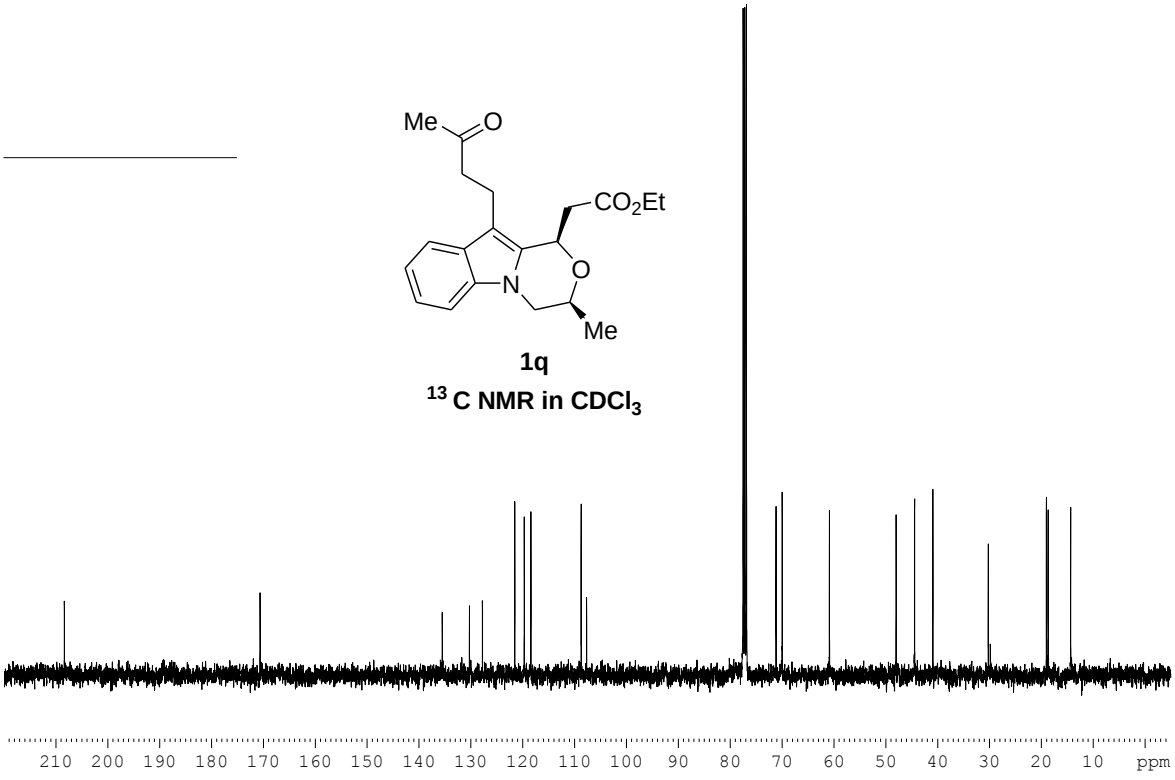

O
CF3
CO2Et
O
N
Me
1p
1H NMR in CDCl3
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
1.041
3.203
1.000
1.389
1.825
1.132
1.097
1.095
1.070
3.251
3.035
1p
13 C NMR in CDCl3
220 200 180 160 140 120 100 80 60 40 20 0 ppm


O
CF3
CO2Et
Hb
N
O
Ha
1p Me
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm
O
CF3
CO2Et
Hb
N
O
Ha
1p Me
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



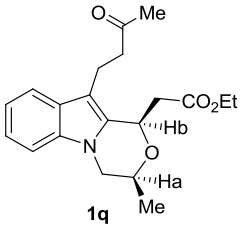
1q

^{1}H NMR in $CDCl_3$



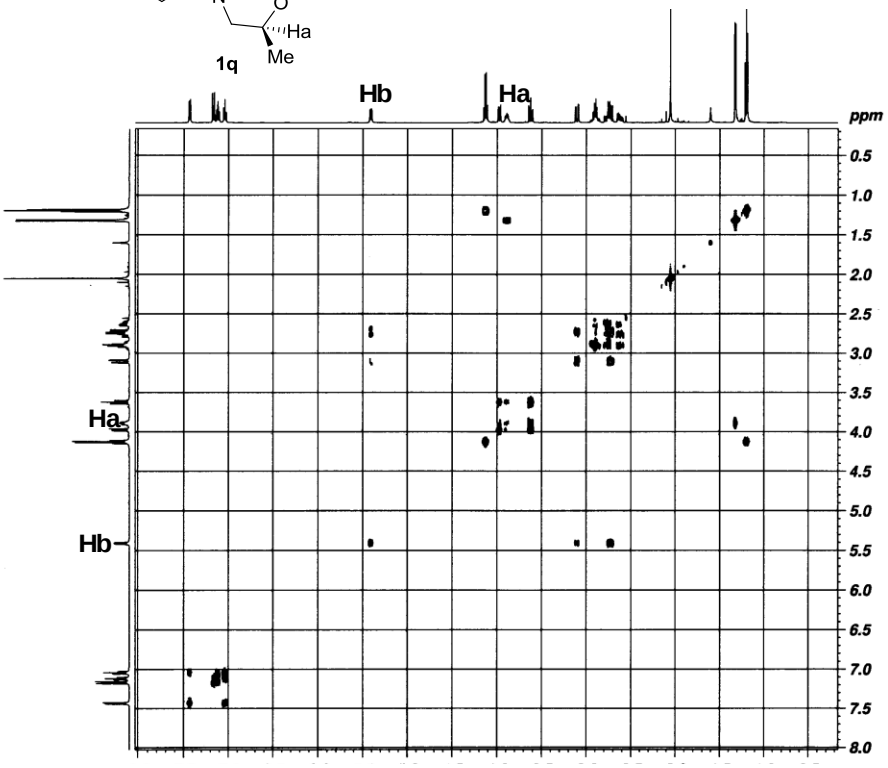
1q

^{13}C NMR in $CDCl_3$



1q

^{1}H-^{1}H COSY and NOESY



Current Data Parameters
NAME Jan21-2010
EXPNO 4
PROCNO 1

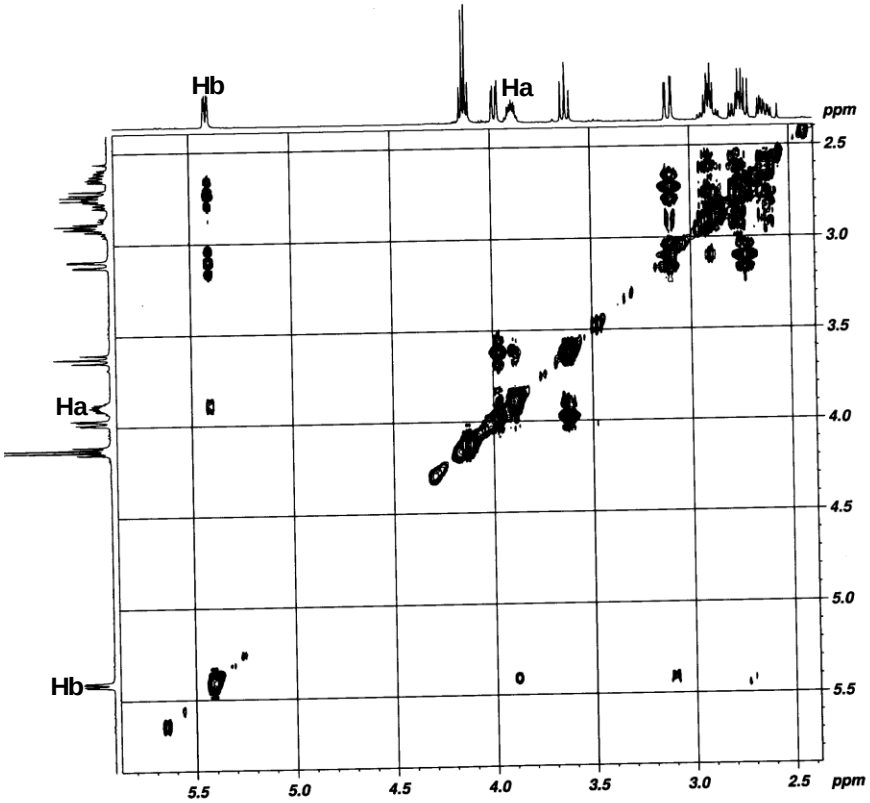
F2 - Acquisition Parameters
Date_ 20100121
Time 23.12
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG cosygpqf
TD 2048
SOLVENT CDCl3
NS 4
DS 8
SWH 3937.008 Hz
FIDRES 1.922367 Hz
AQ 0.2601460 sec
RG 64
DW 127.000 usec
DE 6.50 usec
TE 298.3 K
D0 0.00000300 sec
D1 1.37998605 sec
D13 0.00000400 sec
D16 0.00020000 sec
IN0 0.00025400 sec

======== CHANNEL f1 ========
NUC1 1H
P0 10.65 usec
P1 10.65 usec
PL1 0.00 dB
PL1W 23.53637505 W
SFO1 500.1320985 MHz

====== GRADIENT CHANNEL ==
GPNAM1 SINE.100
GPZ1 10.00 %
P16 1000.00 usec

F1 - Acquisition parameters
ND0 1
TD 128
SFO1 500.1321 MHz
FIDRES 30.757874 Hz
SW 7.872 ppm
FnMODE QF

F2 - Processing parameters
SI 1024
SF 500.1300518 MHz
WDW SINE
SSB 0
LB 0.00 Hz
GB 0
PC 1.40



Current Data Parameters
NAME Jan21-2010
EXPNO 5
PROCNO 1

F2 - Acquisition Parameters
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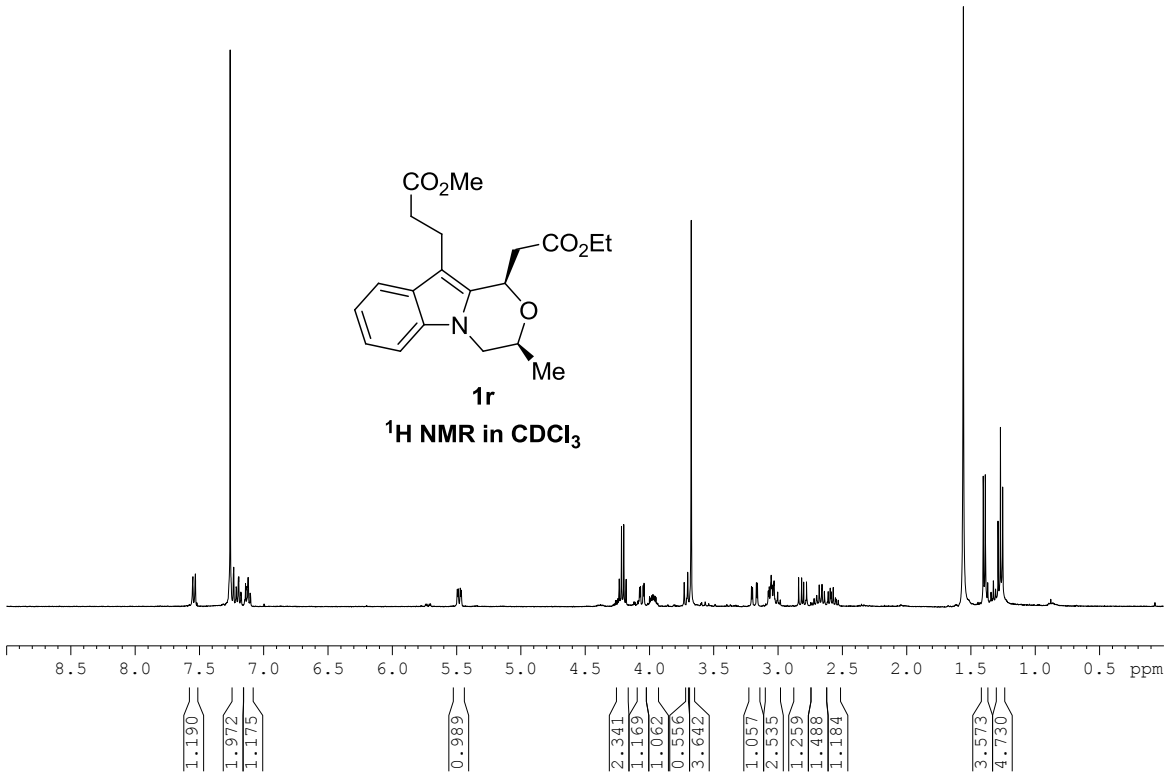
INSTRUM spect
PROBHD 5 mm PABBO BB-
PULPROG noesyph
TD 2048
SOLVENT CDCl3
NS 32
DS 4
SWH 3937.008 Hz
FIDRES 1.922367 Hz
AQ 0.2601460 sec
RG 64
DW 127.000 usec
DE 6.50 usec
TE 298.1 K
D0 0.00011344 sec
D1 1.94060802 sec
D8 0.30000001 sec
IN0 0.00025400 sec

======== CHANNEL f1 ========
NUC1 1H
P1 10.65 usec
PL1 0.00 dB
PL1W 23.53637505 W
SFO1 500.1320985 MHz

F1 - Acquisition parameters
ND0 1
TD 256
SFO1 500.1321 MHz
FIDRES 15.378937 Hz
SW 7.872 ppm
FnMODE States-TPPI

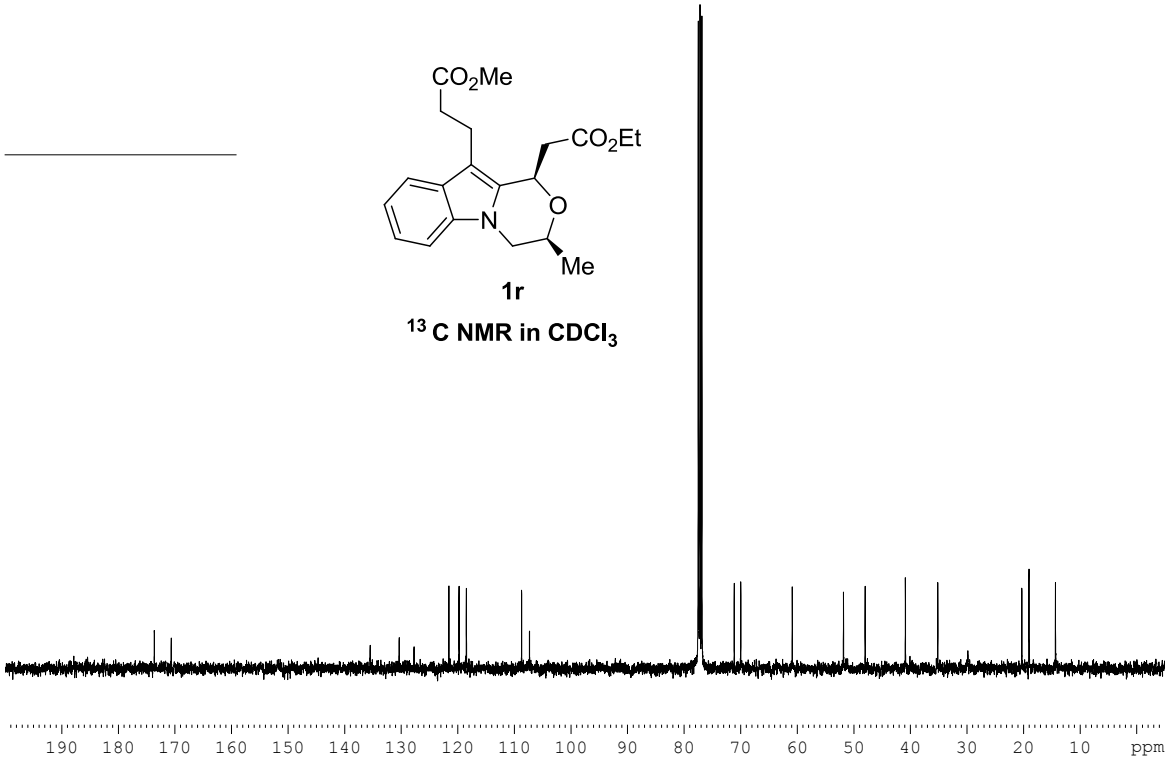
F2 - Processing parameters
SI 1024
SF 500.1300518 MHz
WDW QSINE
SSB 2
LB 0.00 Hz
GB 0
PC 1.00

F1 - Processing parameters
SI 1024
MC2 States-TPPI
SF 500.1300518 MHz
WDW QSINE
SSB 2



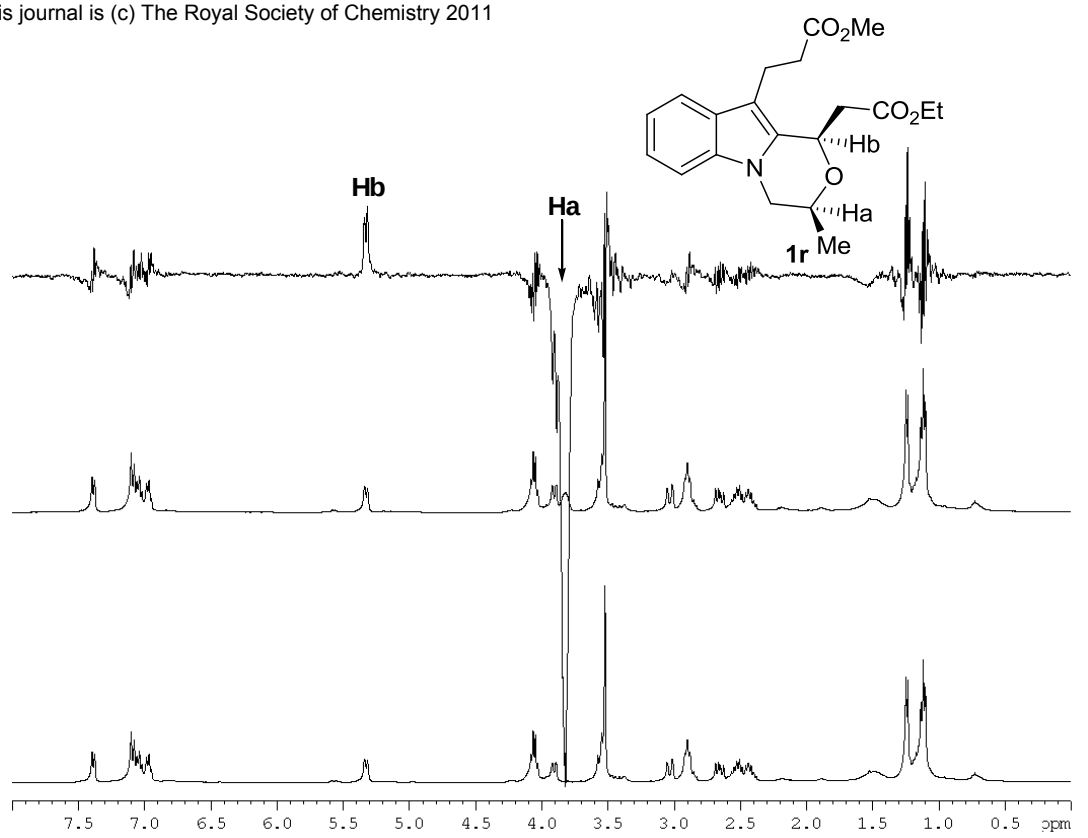
1r

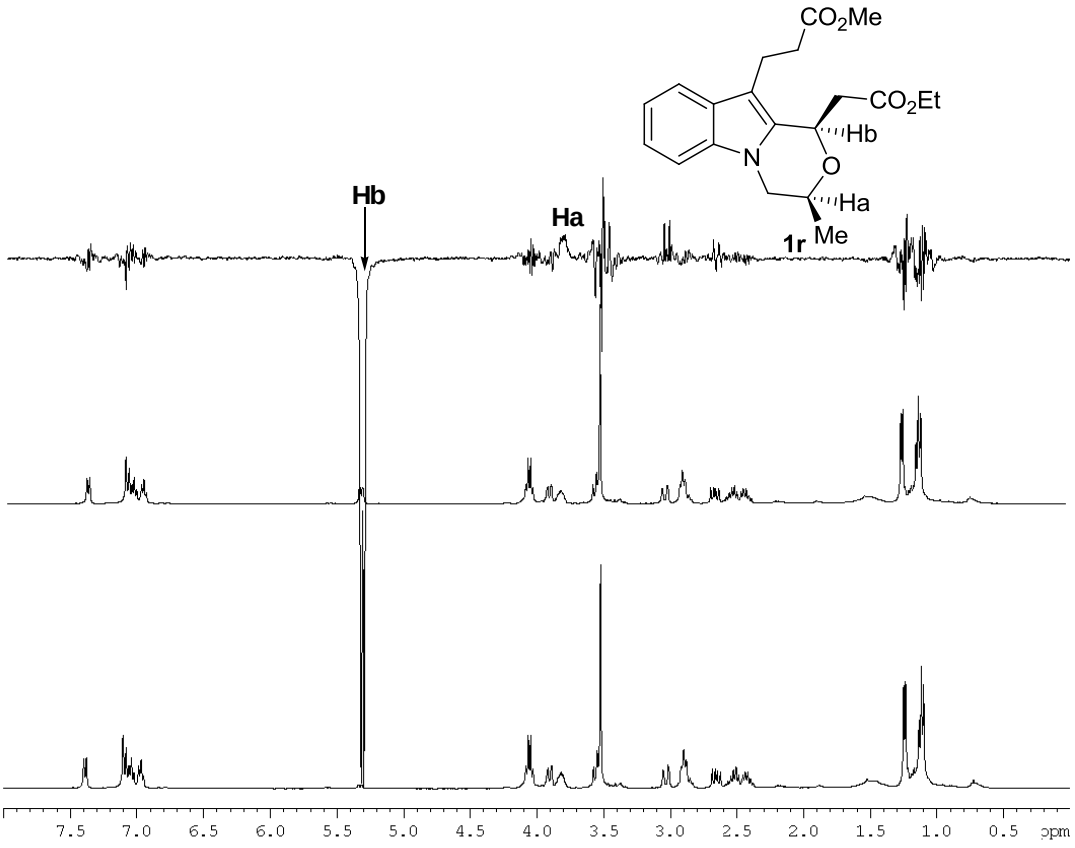
^{1}H NMR in $CDCl_3$

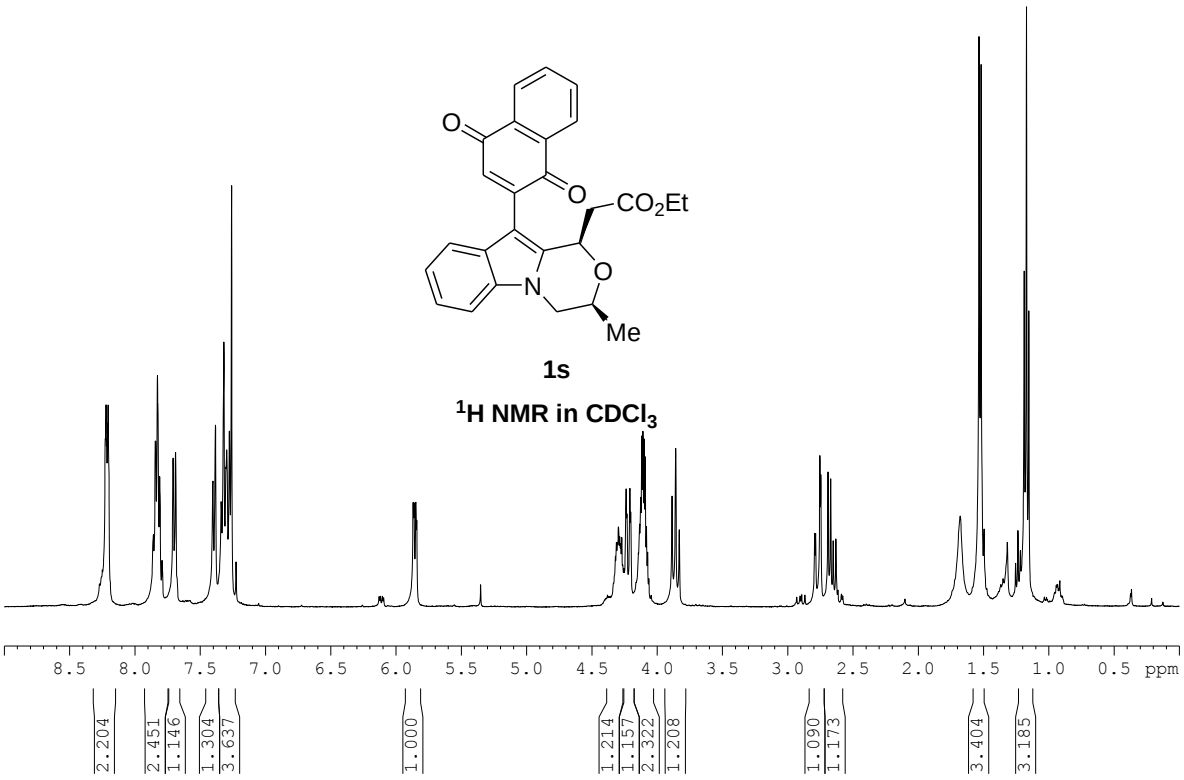


1r

^{13}C NMR in $CDCl_3$

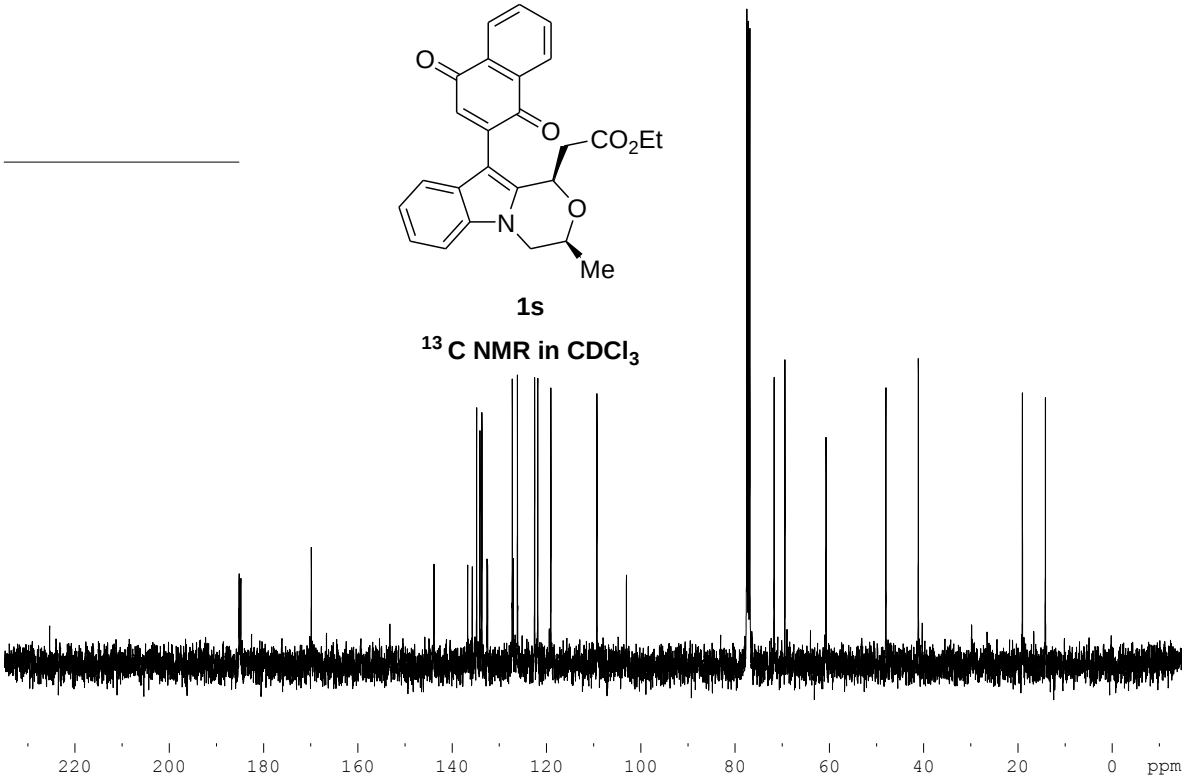

CO2Me
CO2Et
Hb
N
O
Ha
Me
1r
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


CO2Me
CO2Et
Hb
N
O
Ha
Me
1r
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



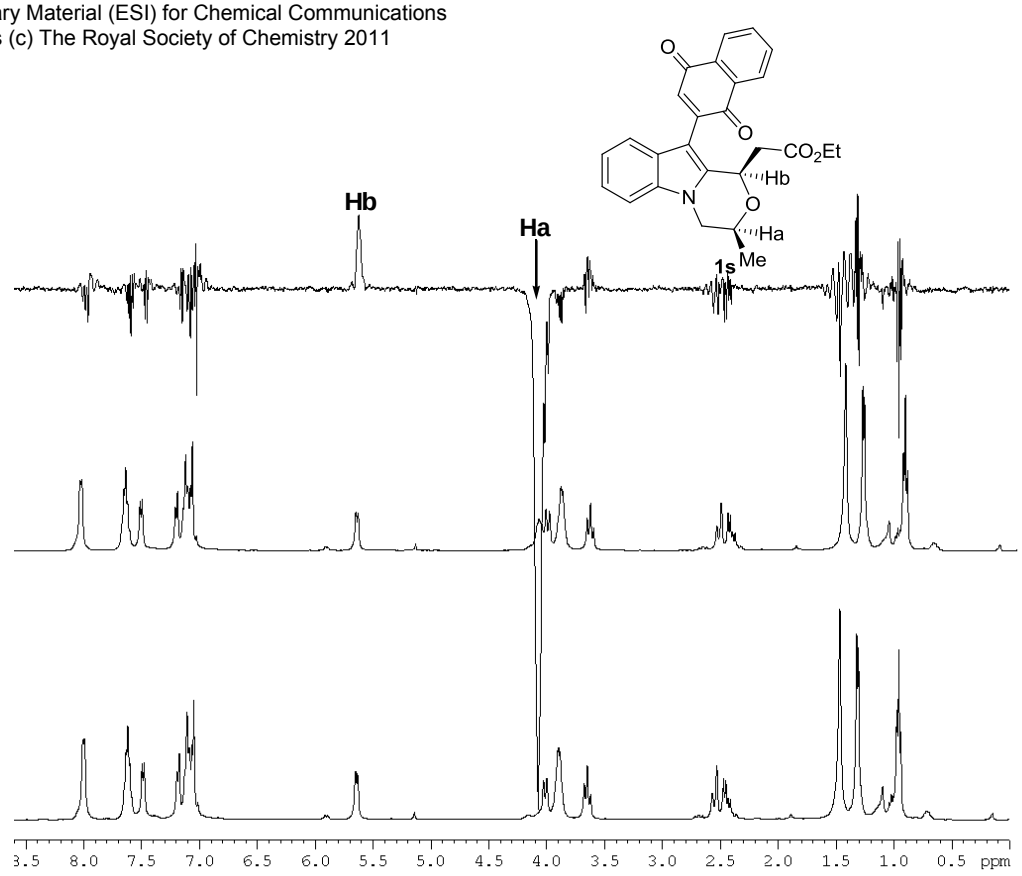
1s

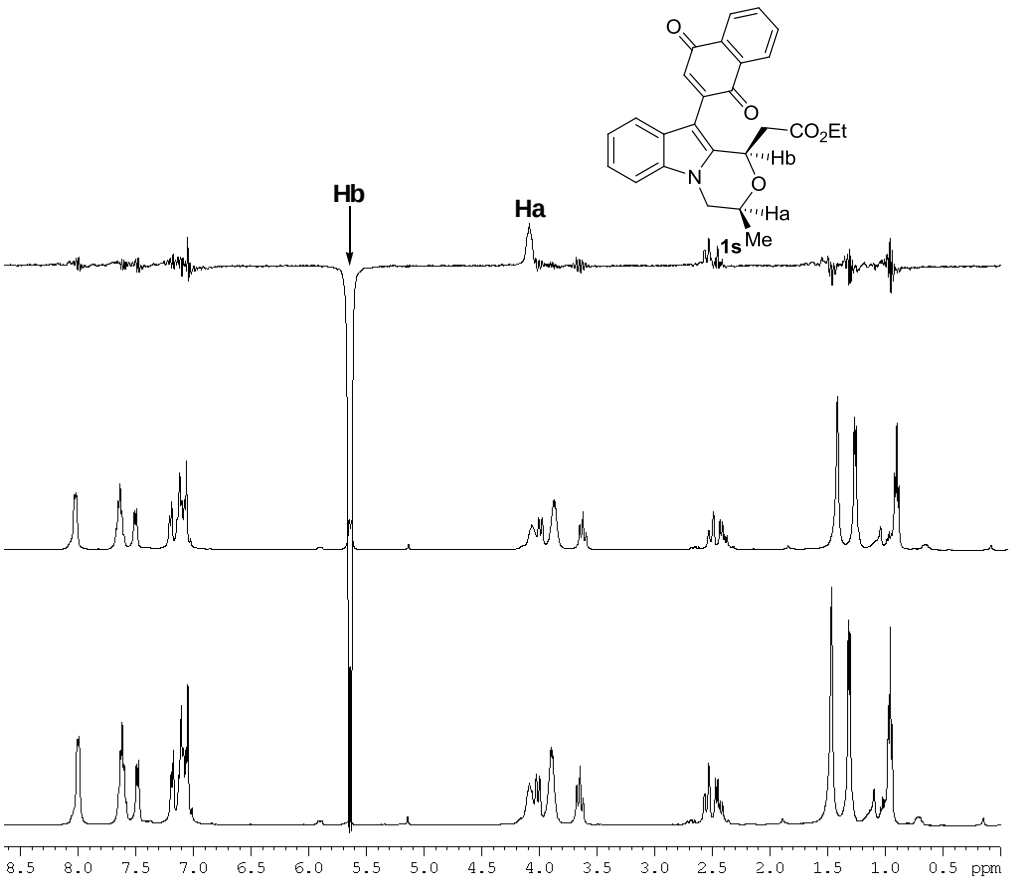
^{1}H NMR in $CDCl_3$

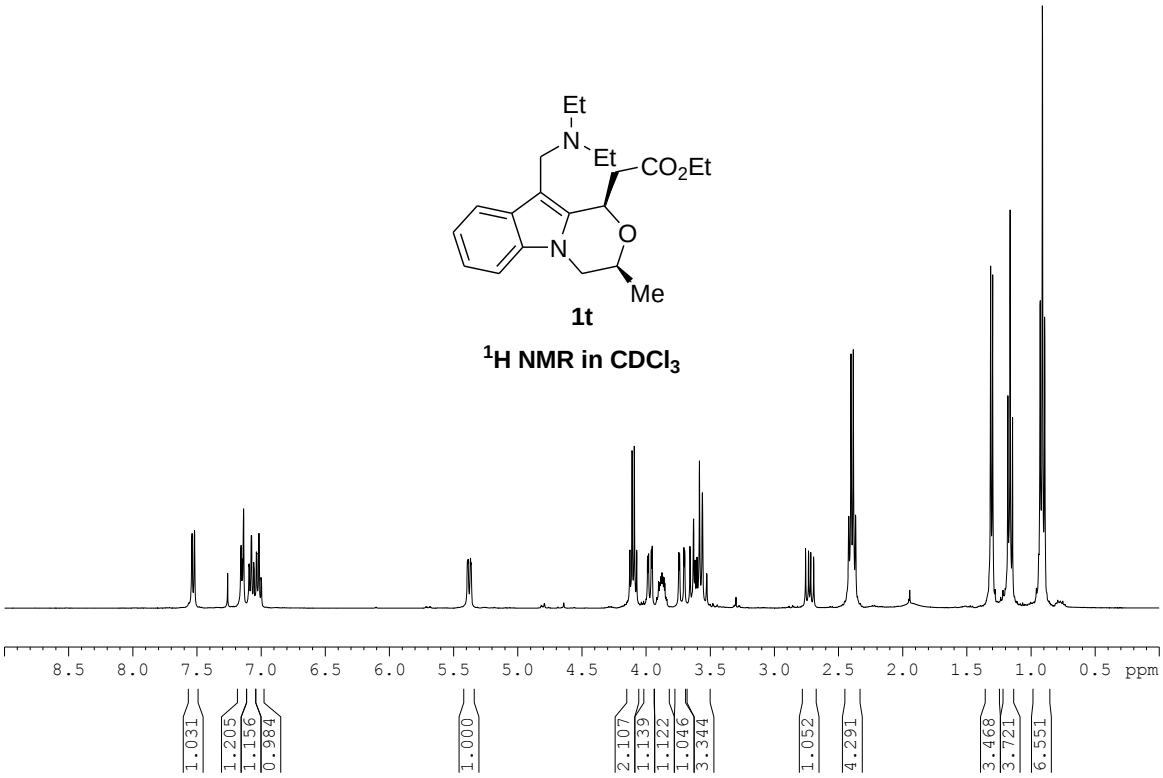


1s

^{13}C NMR in $CDCl_3$

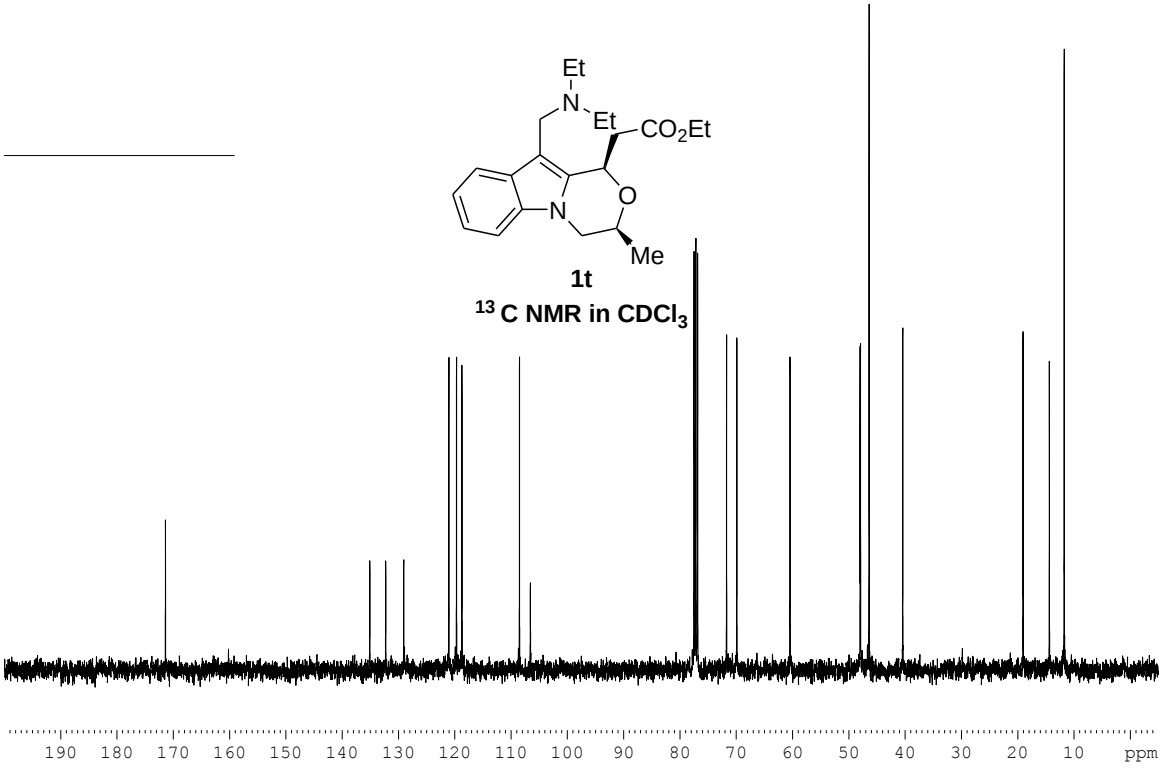

O
O
CO2Et
Hb
N
O
Ha
Me
1s
Hb
Ha
3.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


O
O
CO2Et
Hb
N
O
Ha
Me
1s
Hb
Ha
8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



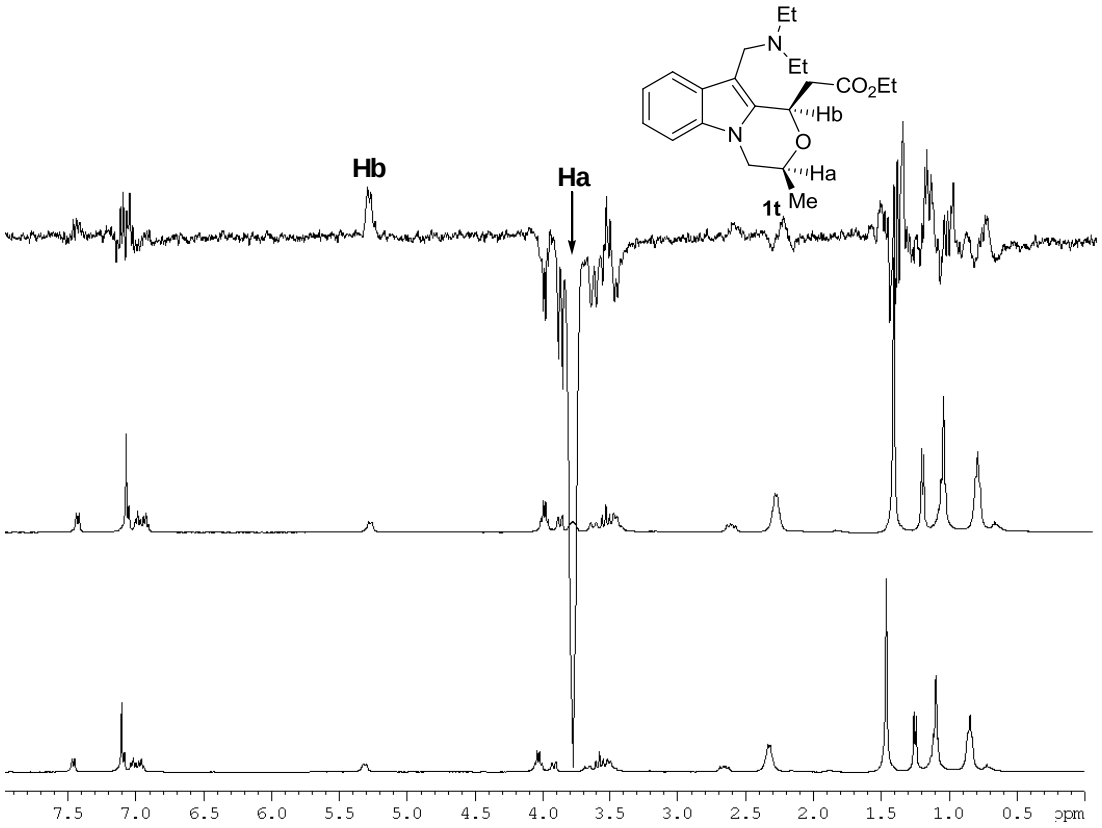
1t

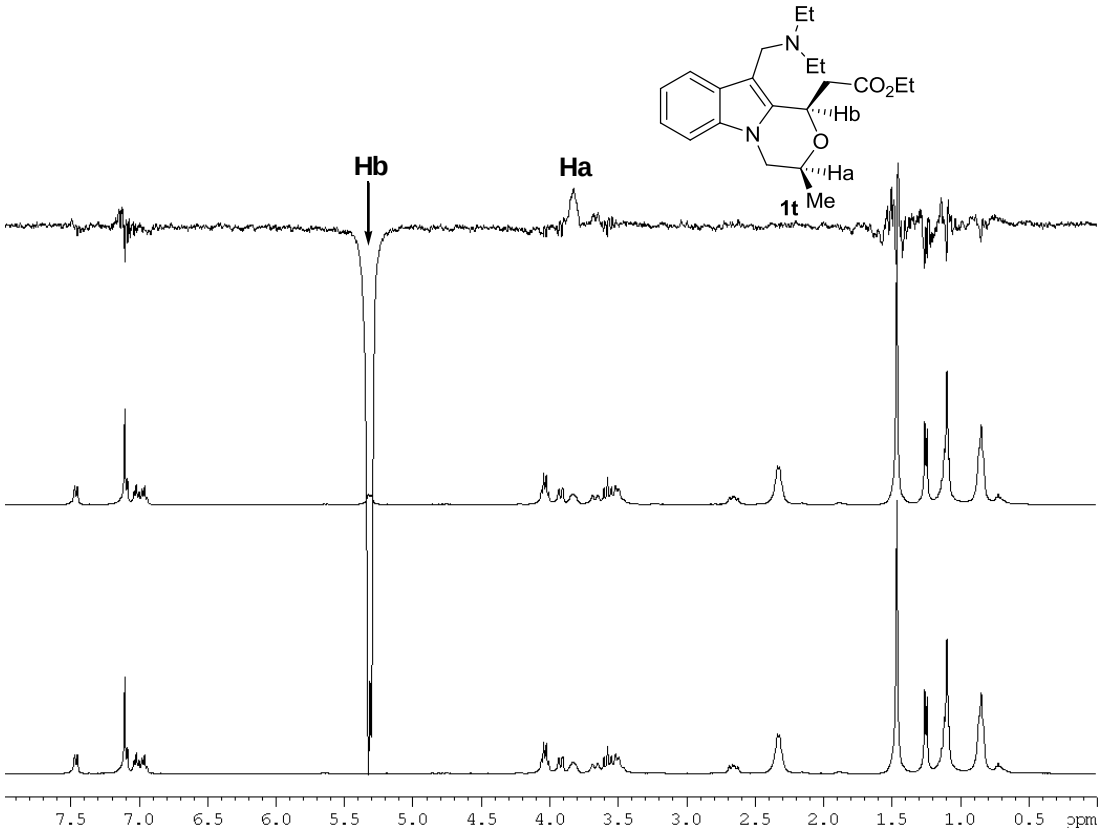
^{1}H NMR in $CDCl_3$

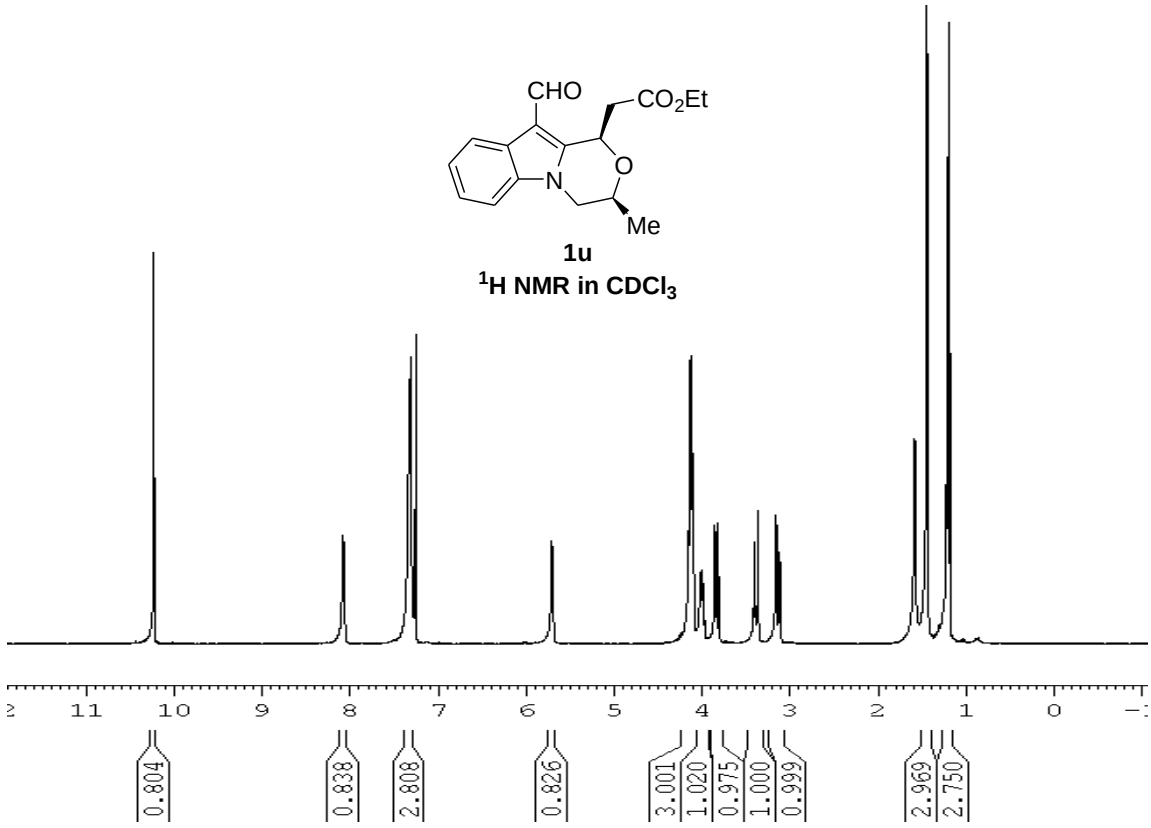


1t

^{13}C NMR in $CDCl_3$

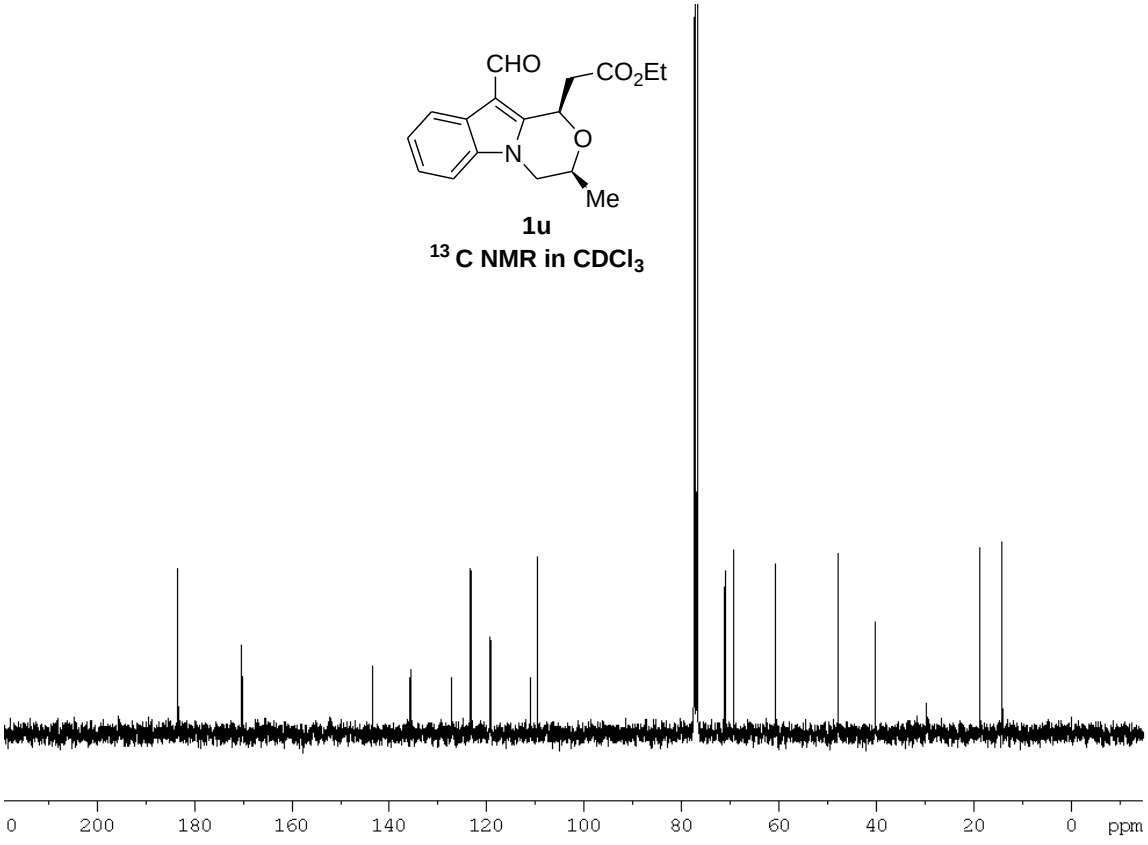

Et
N
Et
CO2Et
Hb
O
Ha
Me
1t
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm


Et
N
Et
CO2Et
Hb
O
Ha
Me
1t
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm



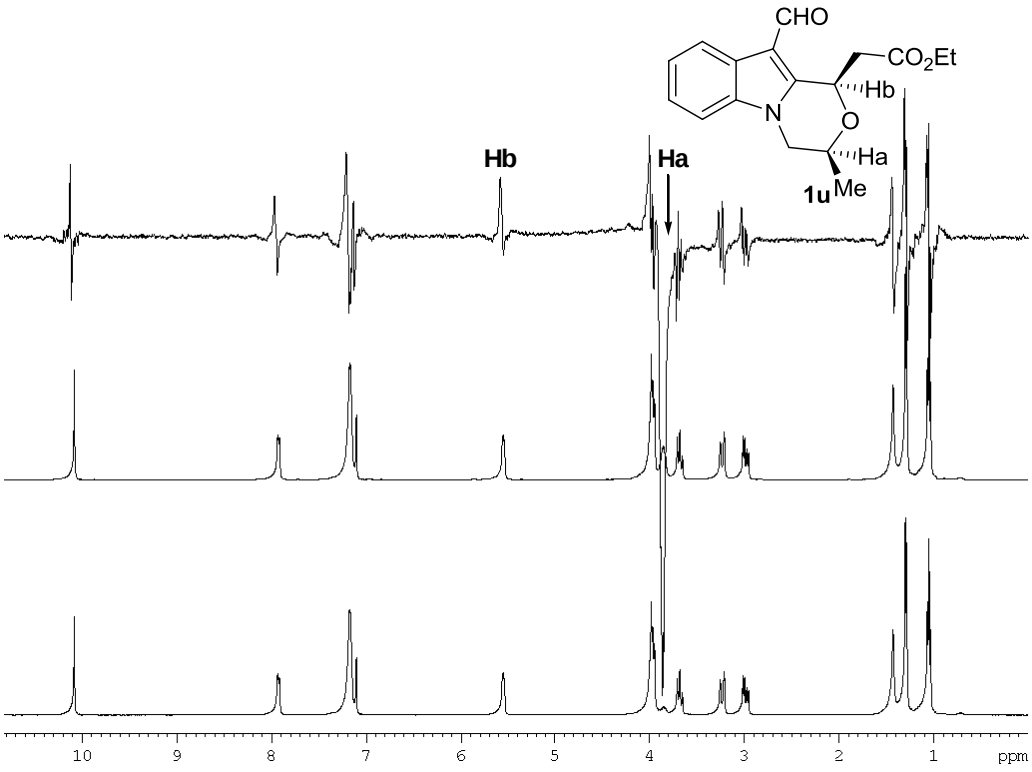
1u

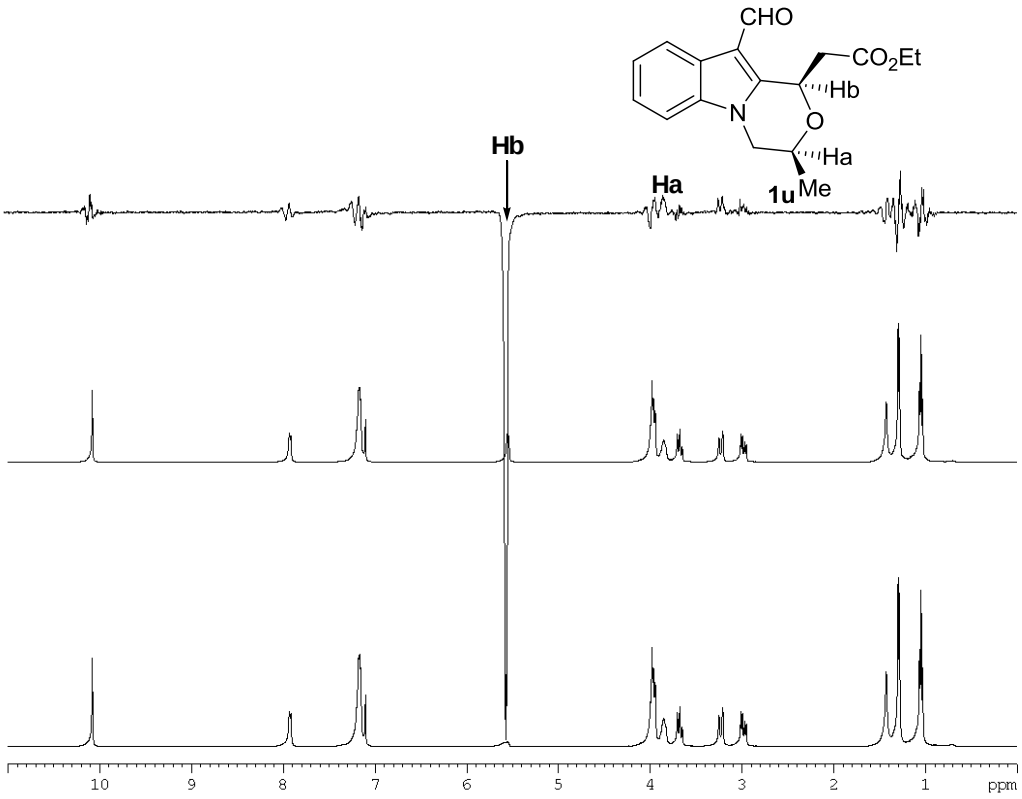
^{1}H NMR in $CDCl_3$

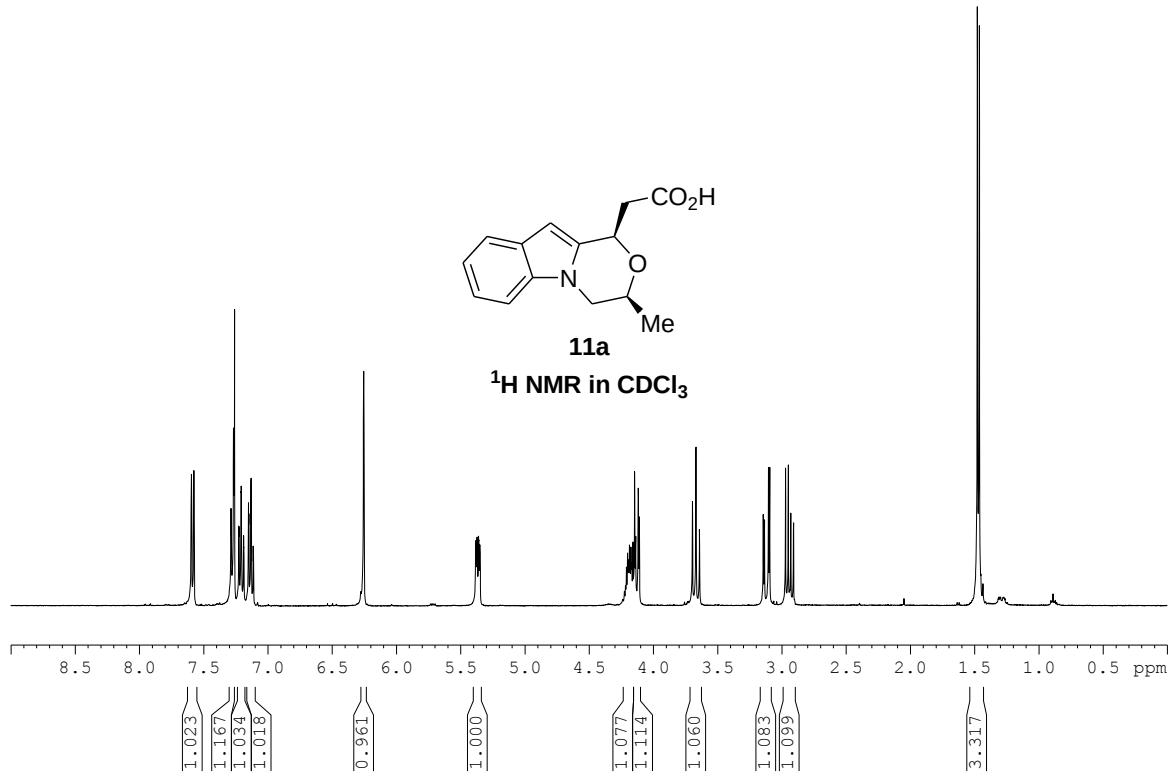


1u

^{13}C NMR in $CDCl_3$

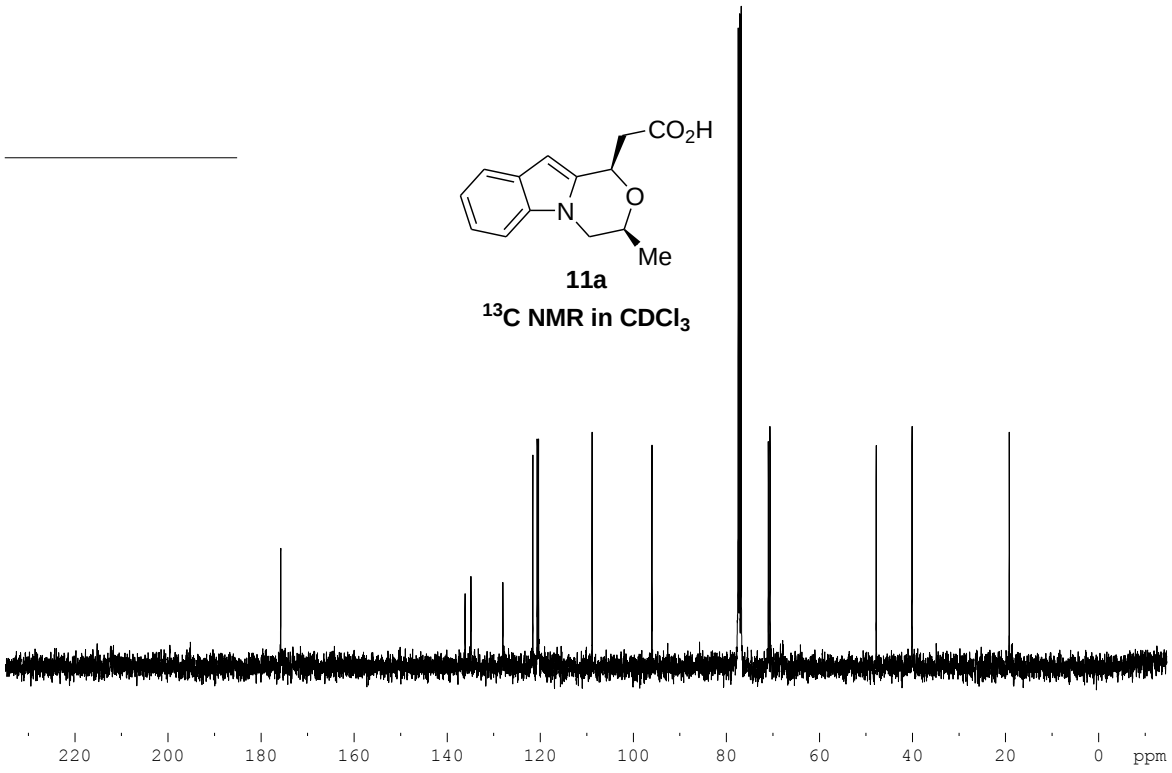

CHO
CO2Et
Hb
N
O
Ha
Me
1u
Hb
Ha
10
9
8
7
6
5
4
3
2
1
ppm


CHO
CO2Et
Hb
N
O
Ha
Me
1u
Hb
Ha
10
9
8
7
6
5
4
3
2
1
ppm



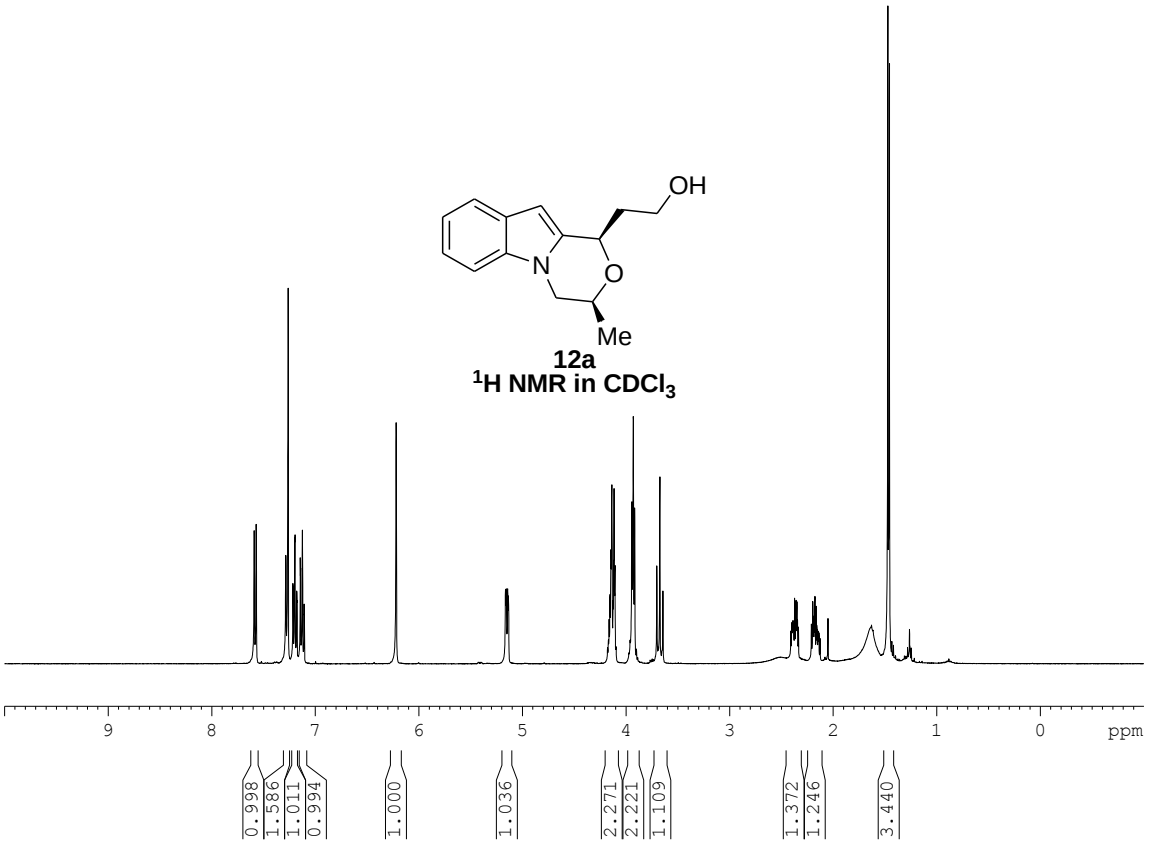
11a

^{1}H NMR in $CDCl_3$

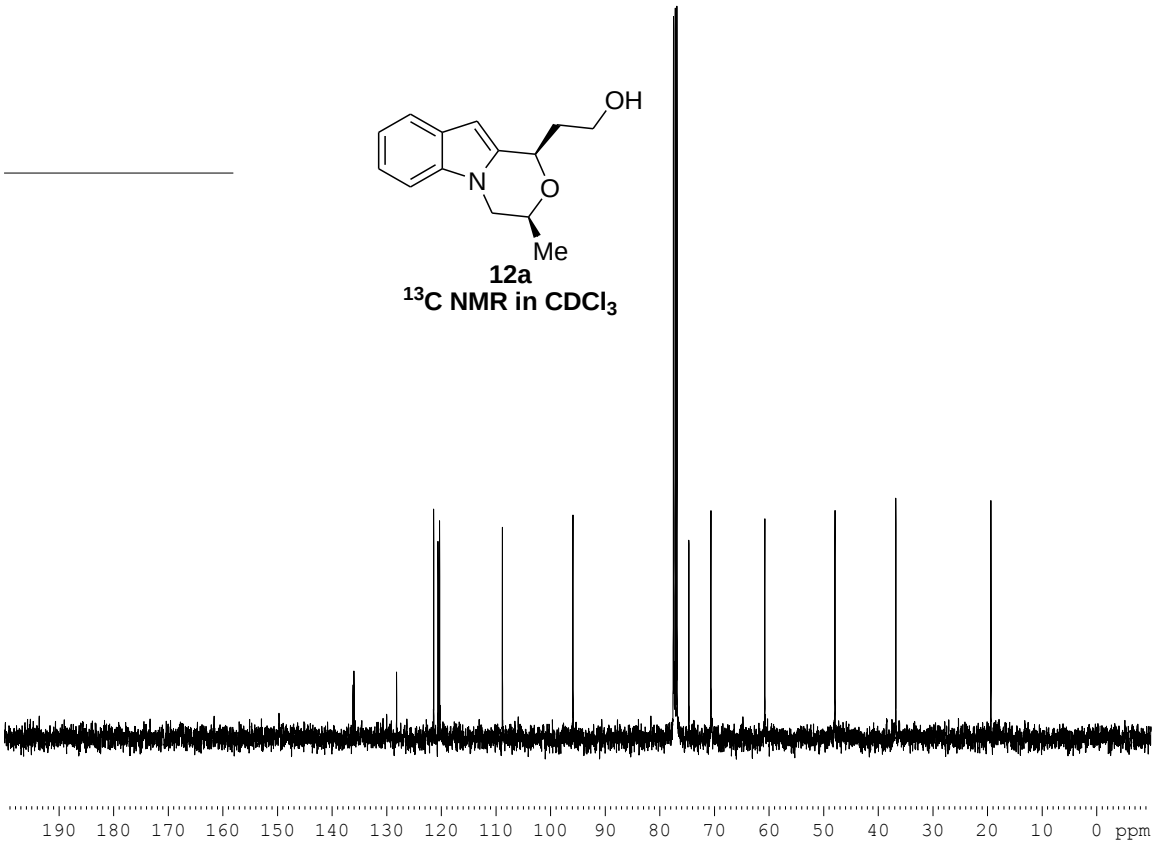


11a

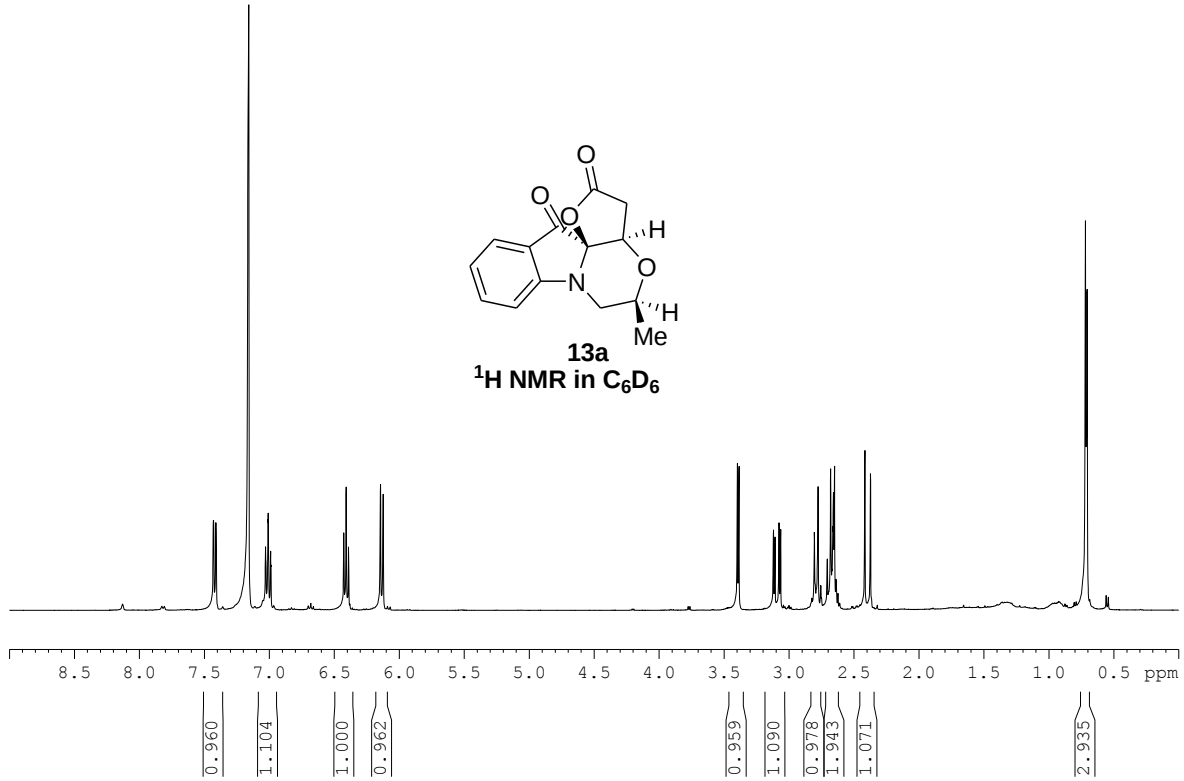
^{13}C NMR in $CDCl_3$



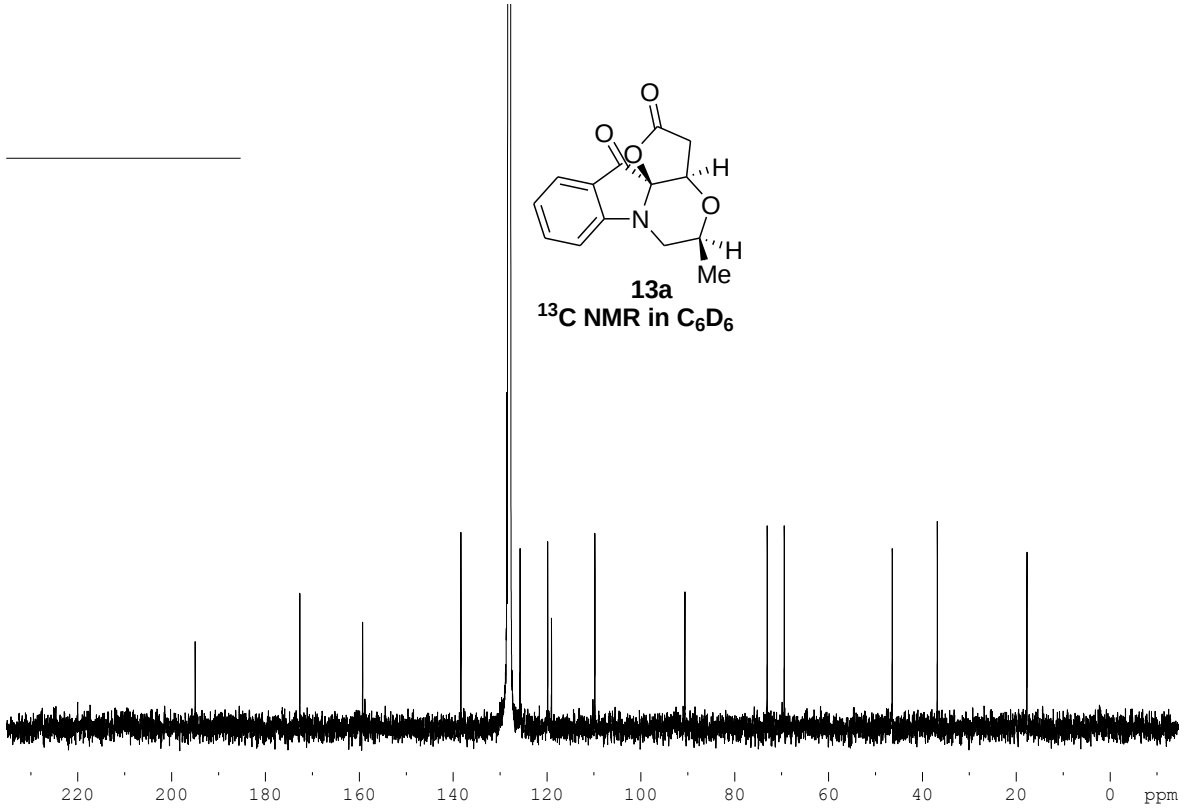
12a
^{1}H NMR in $CDCl_3$



12a
^{13}C NMR in $CDCl_3$

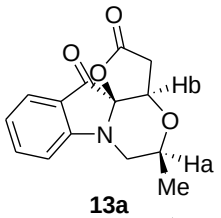


13a
^{1}H NMR in C_6D_6

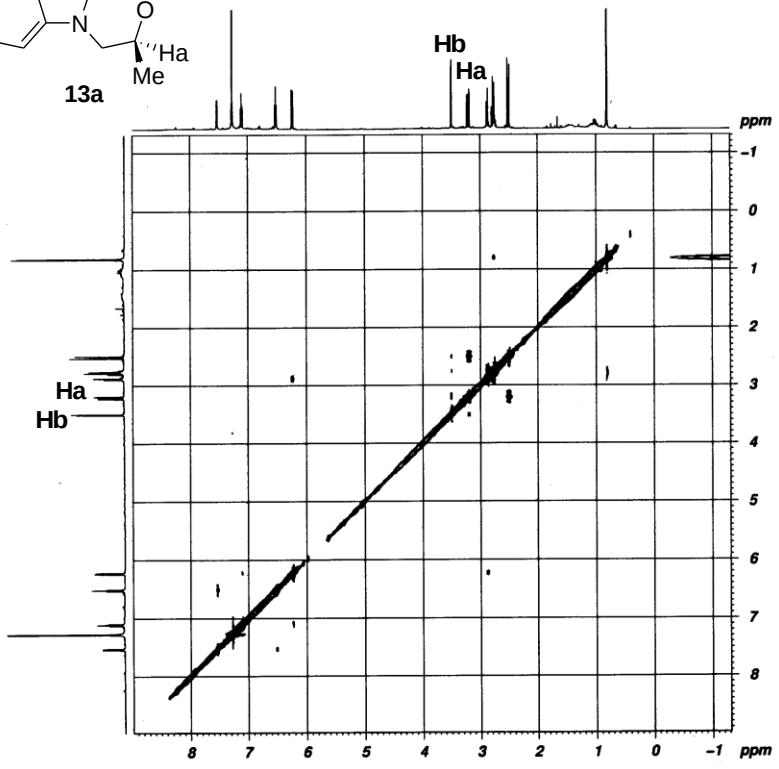


13a
^{13}C NMR in C_6D_6

^{1}H-^{1}H COSY and NOESY



13a

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EXPNO                    3
PROCNO                   1
Date_             20100120
Time                 18.12
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG             noesyph
TD                    2048
SOLVENT               C6D6
NS                      32
DS                       4
SWH               5154.639 Hz
FIDRES            2.516914 Hz
AQ                0.1987060 sec
RG                      64
DW                97.000 usec
DE                 6.50 usec
TE                 297.4 K
D0              0.00008344 sec
D1              2.00204802 sec
D8              0.30000001 sec
IN0             0.00019400 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                 10.65 usec
PL1                 0.00 dB
PL1W          23.53637505 W
SFO1          500.1319160 MHz
ND0                      1
TD                     256
SFO1            500.1319 MHz
FIDRES          20.135309 Hz
SW                10.307 ppm
FnMODE       States-TPPI
SI                    1024
SF            500.1300000 MHz
WDW                 QSINE
SSB                      2
LB                 0.00 Hz
GB                       0
PC                    1.00
SI                    1024
MC2          States-TPPI
SF            500.1300000 MHz
WDW                 QSINE
SSB                      2
LB                 0.00 Hz
GB                       0
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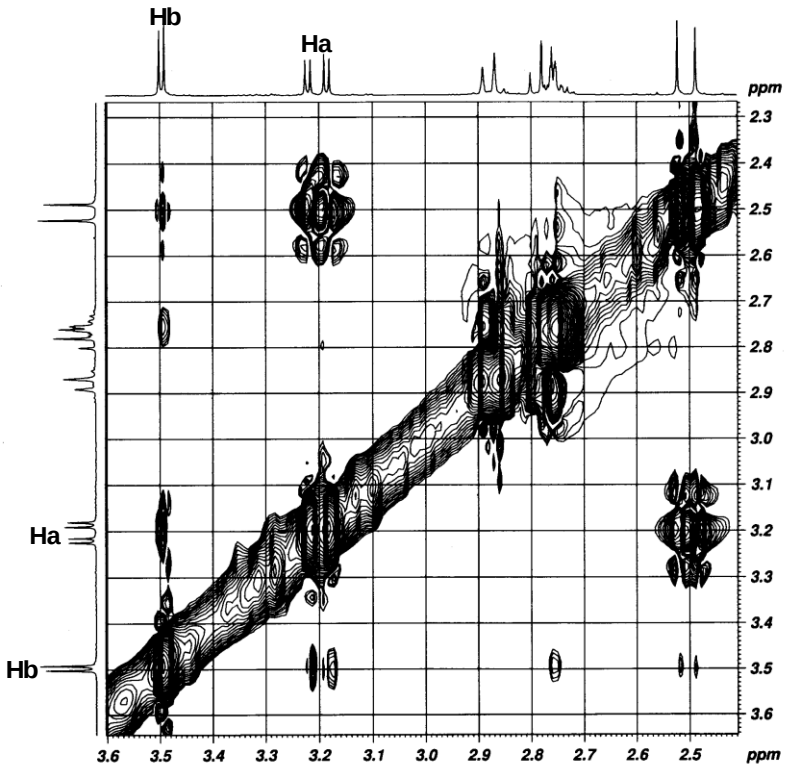


```
NAME            Jan20-2010
EXPNO                    3
PROCNO                   1
Date_             20100120
Time                 18.12
INSTRUM              spect
PROBHD   5 mm PABBO BB-
PULPROG             noesyph
TD                    2048
SOLVENT               C6D6
NS                      32
DS                       4
SWH               5154.639 Hz
FIDRES            2.516914 Hz
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======== CHANNEL f1 ========
NUC1                    1H
P1                 10.65 usec
PL1                 0.00 dB
PL1W          23.53637505 W
SFO1          500.1319160 MHz
ND0                      1
TD                     256
SFO1            500.1319 MHz
FIDRES          20.135309 Hz
SW                10.307 ppm
FnMODE       States-TPPI
SI                    1024
SF            500.1300000 MHz
WDW                 QSINE
SSB                      2
LB                 0.00 Hz
GB                       0
PC                    1.00
SI                    1024
MC2          States-TPPI
SF            500.1300000 MHz
WDW                 QSINE
SSB                      2
LB                 0.00 Hz
GB                       0
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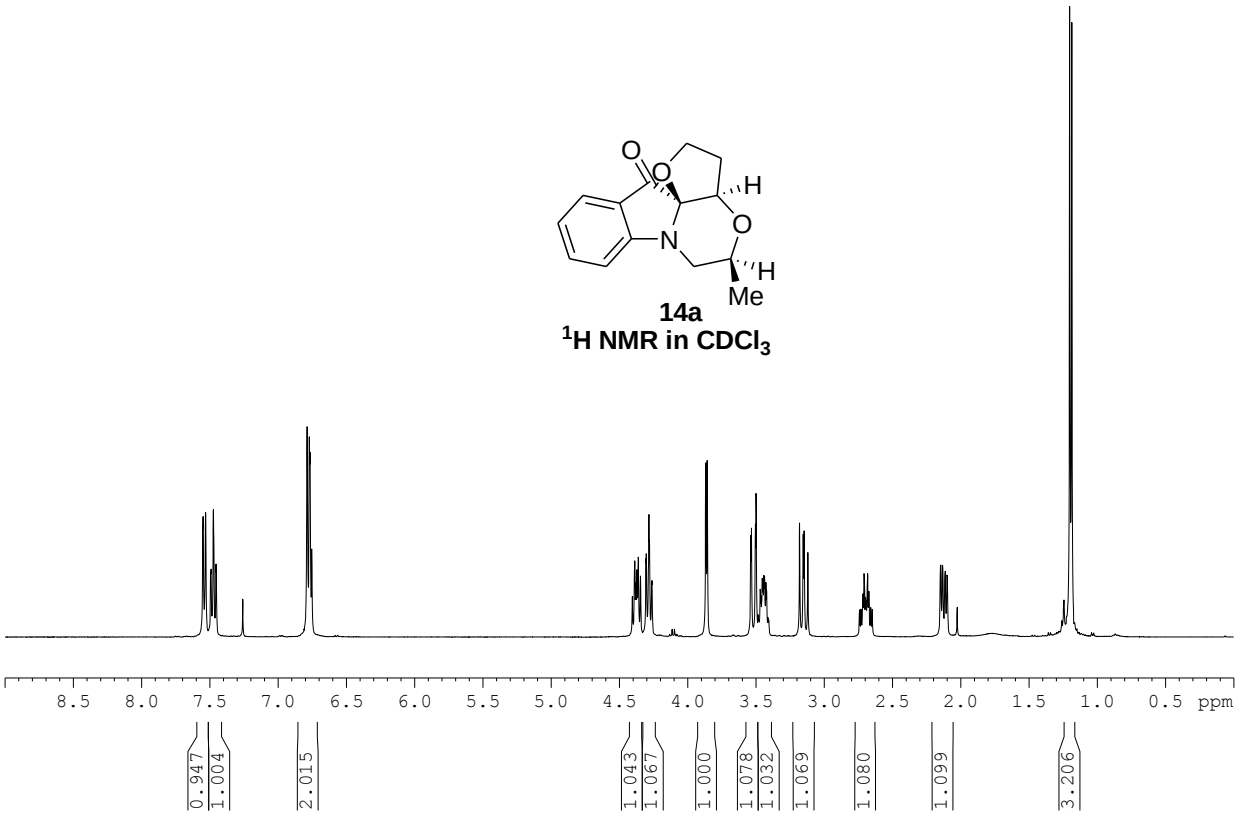
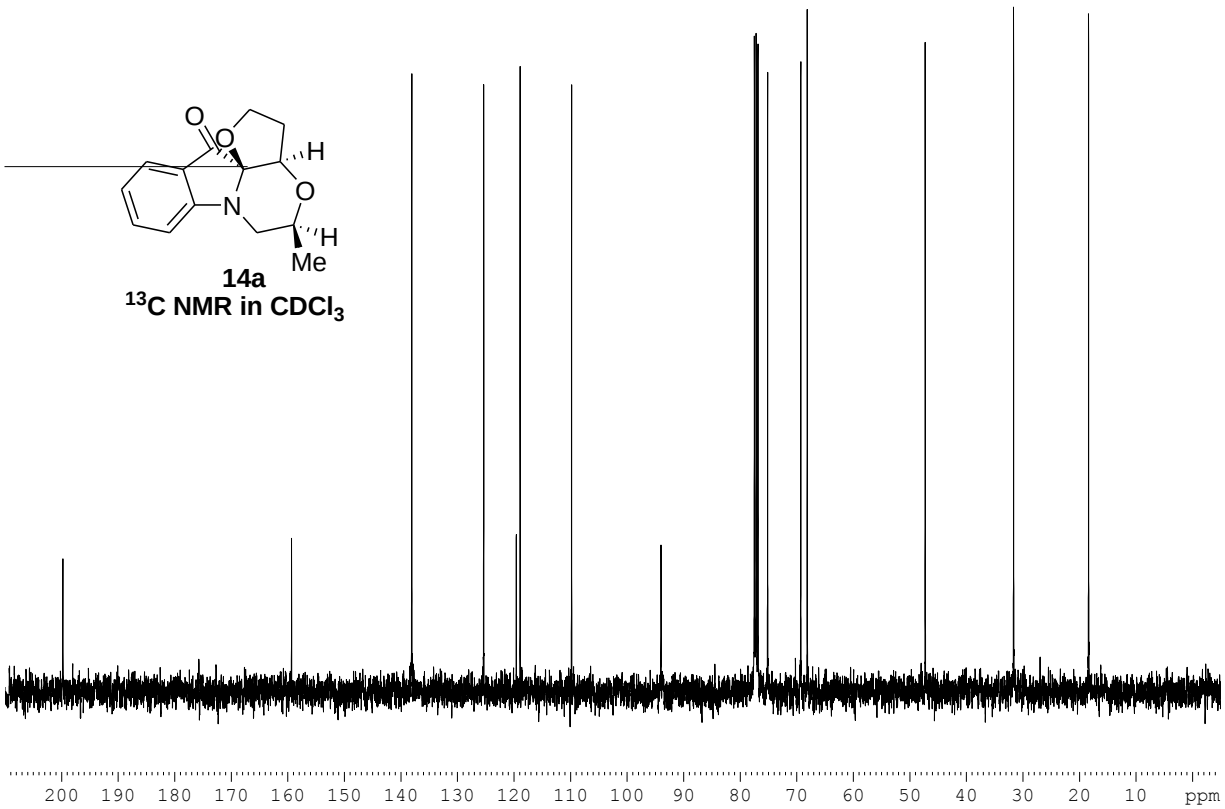
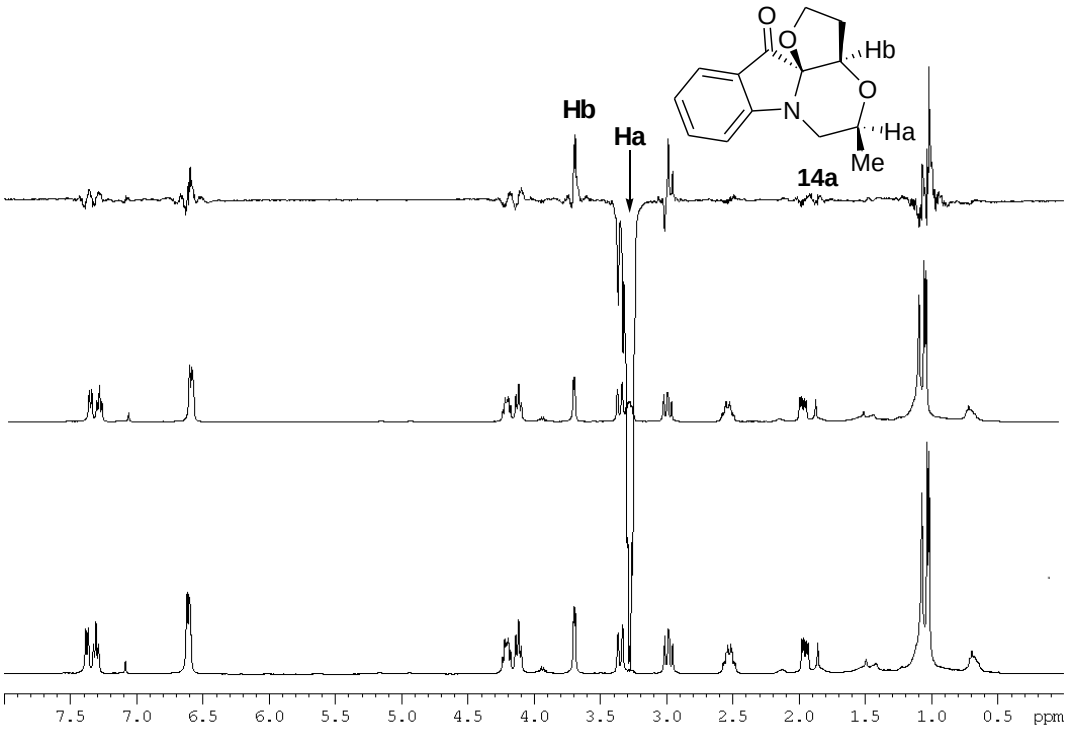
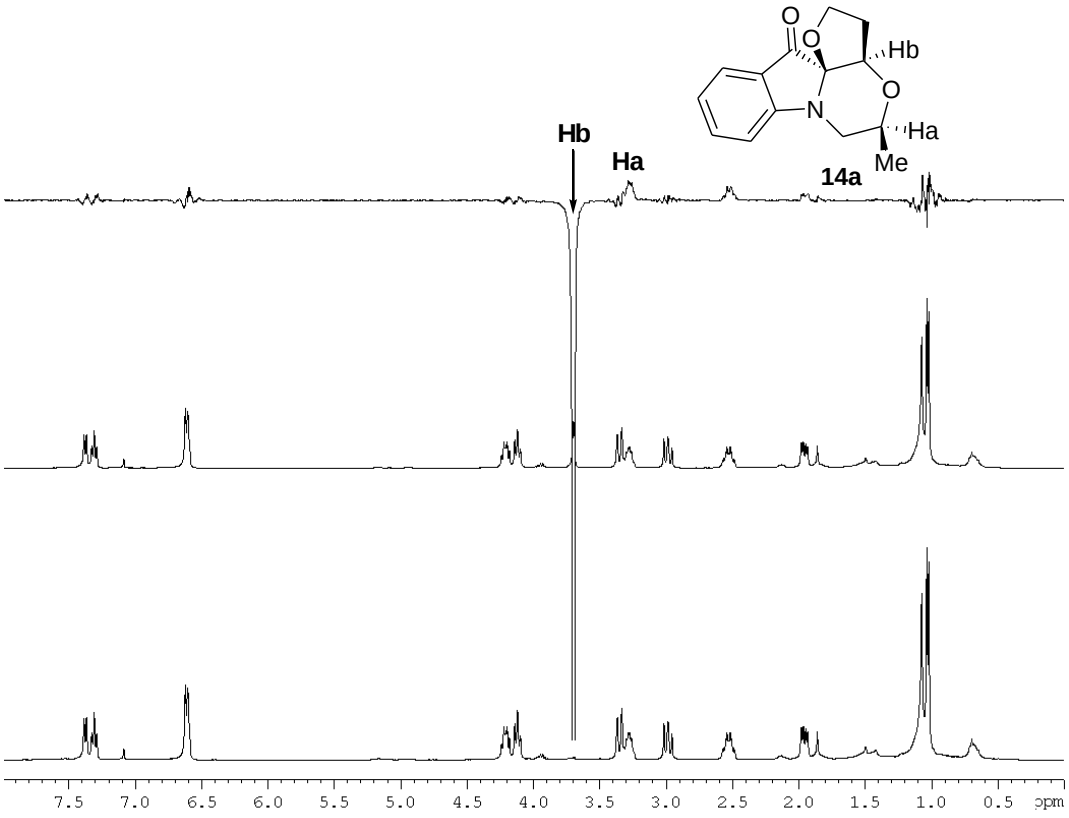


14a
^{1}H NMR in $CDCl_3$

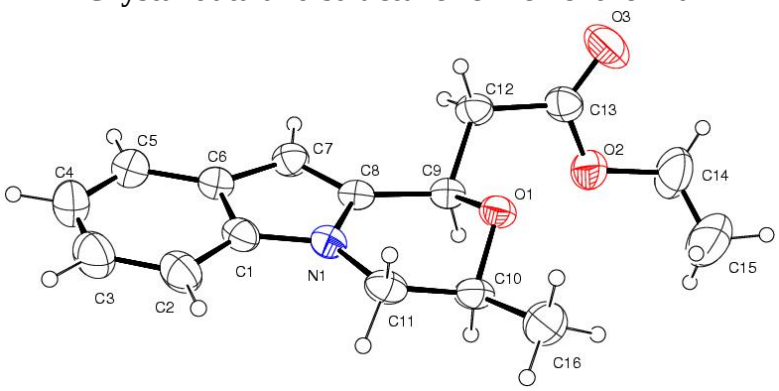


14a
^{13}C NMR in $CDCl_3$


O
O
Hb
O
N
Ha
Me
14a
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

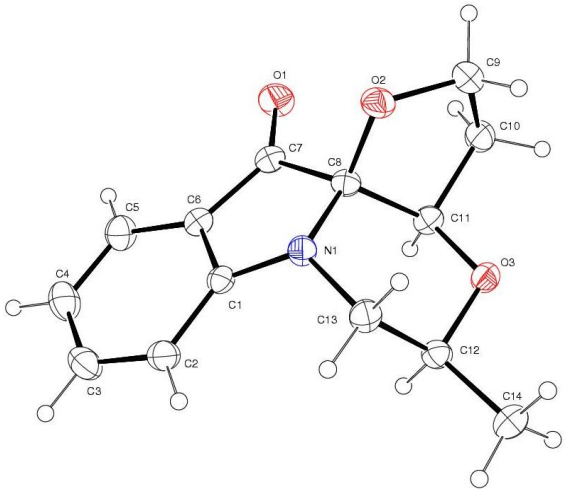

O
O
Hb
O
N
Ha
Me
14a
Hb
Ha
7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 ppm

Crystal data and structure refinement for 1a



CCDC No.	801688
Identification code	**1a**
Empirical formula	C16 H20 N O3
Formula weight	274.33
Temperature	298(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 10.4764(4) A alpha = 90 deg. b = 8.4739(3) A beta = 102.944(2) deg. c = 17.5527(8) A gamma = 90 deg.
Volume	1518.66(11) A^3
Z, Calculated density	4, 1.200 Mg/m^3
Absorption coefficient	0.083 mm^-1
F(000)	588
Crystal size	0.38 x 0.22 x 0.20 mm
Theta range for data collection	2.54 to 29.06 deg.
Limiting indices	-14<=h<=12, -8<=k<=11,21<=l<=23
Reflections collected / unique	12548 / 3748 [R(int) = 0.0268]
Completeness to theta = 25.00	96.8 %
Absorption correction	None
Max. and min. transmission	0.9837 and 0.9693
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3748 / 0 / 184
Goodness-of-fit on F^2	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0707, wR2 = 0.2112
R indices (all data)	R1 = 0.1213, wR2 = 0.2508
Extinction coefficient	0.006(4)
Largest diff. peak and hole	0.392 and -0.518 e.A^-3

Crystal data and structure refinement for 14a



CCDC No. 801689	
Identification code	**14a**
Empirical formula	C14 H15 N O3
Formula weight	245.27
Temperature	298(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)/c
Unit cell dimensions	a = 6.05110(10) A alpha = 90 deg. b = 14.5244(5) A beta = 100.186(2) deg. c = 14.0584(5) A gamma = 90 deg.
Volume	1216.10(6) A^3
Z, Calculated density	4, 1.340 Mg/m^3
Absorption coefficient	0.095 mm^-1
F(000)	520
Crystal size	0.35 x 0.28 x 0.15 mm
Theta range for data collection	3.17 to 28.30 deg.
Limiting indices	-7<=h<=6, -15<=k<=19, -18<=l<=16
Reflections collected / unique	8987 / 2805 [R(int) = 0.0323]
Completeness to theta = 25.00	96.5 %
Absorption correction	None
Max. and min. transmission	0.9860 and 0.9677
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2805 / 0 / 164
Goodness-of-fit on F^2	0.901
Final R indices [I>2sigma(I)]	R1 = 0.0440, wR2 = 0.1207
R indices (all data)	R1 = 0.0749, wR2 = 0.1434
Largest diff. peak and hole	0.216 and -0.191 e.A^-3